Blood Substitutes

Baxter Healthcare Corporation
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

847.270.5300
Fax: 847.270.5306

Baxter

September 15, 1997

9927 '97 SEP 18 A9:49

Docket Number 95S-0158
Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Dr. rm. 1-23
Rockville, MD 20857

RE: Investigational New Drug Application #6859

Dear Sir/Madam:

In accordance with 21 CFR §312.54 we are enclosing copies of information concerning research involving an exception to informed consent. This includes information that has been publicly disclosed by the IRB at R.A. Cowley Shock Trauma Center, Baltimore, MD, the IRB at Allegheny University of the Health Sciences, Philadelphia, PA, the IRB at Memorial Medical Center, Inc., Savannah, GA, the IRB at Richland Memorial Hospital, Columbia, SC, and additional information from Lehigh Valley Hospital, Allentown, PA.

The information from R.A. Cowley Shock Trauma Center includes the agenda (Attachment 1), meeting minutes (Attachment 2) and a handout (Attachment 3) from a community meeting with Concerned Citizens of Poppleton on April 9, 1997; an article regarding the community meeting that appeared in a local newspaper, *The Baltimore Sun* on April 19, 1997 (Attachment 4); transcripts from television broadcasts which aired on April 19, 1997 on two local stations, WBAL-TV(NBC) (Attachment 5) and WBFF-TV(FOX) (Attachment 6); a letter to the editor of a local newspaper, *The Baltimore Sun,* that appeared on May 2, 1997 (Attachment 7); a transcript from an interview with the principal investigator and select IRB members that was broadcast on a local television station, WJZ-TV(CBS) on May 2, 1997 (Attachment 8); and a press release (Attachment 9) and resulting advertisement that appeared in four local newspapers, *The City Paper* (Attachment 10), *The Baltimore Afro-American* (Attachment 11), *The Baltimore Sun,* and *The Baltimore Times* (not included). In accordance with 21 CFR §312.54, this information is also being submitted to the IND file.

Based on information received from the clinical site, the investigator and IRB achieved community consultation by holding a community meeting (Attachment 1, 2, 3), and by printing advertisements that solicited communications from community members and provided information for contacting

95S-0158

SUP 7

the principal investigator and the IRB (Attachment 10, 11).

The information from Allegheny University of the Health Sciences includes minutes from a Community Consultation Meeting held on March 7, 1997 (Attachment 12), as well as a transcript from this meeting (Attachment 13); minutes from a Community Consultation Meeting held on March 24, 1997 (Attachment 14); a transcript of a local talk radio program, called "Medical Frontiers" that was broadcast on WWDB 96.5 FM on March 26, 1997 from 8:00 - 9:00 PM, featuring the principle investigator and the chairperson of the IRB (Attachment 15); a copy of an announcement of community meetings (Attachment 16) that was posted in the Emergency Room, outpatient clinics, and area health district offices, and also published in the following local newspapers: *The Roxborough Review* (2 times), the *Germantown Courier/Mt. Airy Times* (4 times), *The Chestnut Hill Local* (1 time), *The Philadelphia Tribune* (4 times), *the Philadelphia Inquirer City Zone/Philadelphia Daily News* (4 times), *The Philadelphia Inquirer - PA West* (1 time), and *The Philadelphia New Observer* (2 times); transcripts from these Community Meetings held on April 11, 1997 (Attachment 17), April 16, 1997 (Attachment 18), and April 17, 1997 (Attachment 19); a letter that was posted in the Emergency Room, outpatient clinics, and area health district offices, and also sent out to approximately 400 key community members in April, 1997 (Attachment 20); an article that was published in local newspapers, *King of Prussia Post,* on April 10, 1997, *The Valley Item*, on April 17, 1997, and *The Fallser*, on April 18, 1997 (Attachment 21); an article that was published in a local newspaper, the *Germantown Courier* (Attachment 22); an article that was published in the Allegheny University Hospitals newspaper, *InnerView,* in April, 1997 (Attachment 23); an abstract submitted by the principal investigator to the EAST Association (Attachment 24); and a copy of a public service announcement (Attachment 25) that was sent to radio and television stations (list, Attachment 26). In accordance with 21 CFR §312.54, this information is also being submitted to the IND file.

Based on information received from the clinical site, the investigator and IRB achieved community consultation by holding various Community Consultation Meetings (Attachment 17, 18, 19), and by including an 800 number on the advertisement for the community meetings that solicited communications from community members (Attachment 16). In addition, a letter was sent to various community members inviting them to attend the community meetings (Attachment 20), and a public service announcement (Attachment 25) was sent to various radio and television stations (Attachment 26) for public broadcast, which included an 800 number to obtain additional information..

The information from Memorial Medical Center, Inc. includes a press release (Attachment 27) that was received by more than 45 surrounding area hospitals (list of hospitals, Attachment 28); an advertisement that was published in a local newspaper, the *Savannah Morning News*, on August 1 and 3, 1997, and also distributed as a flyer to all of the hospital personnel (Attachment 29); an article that was published in a local newspaper, *the Georgia Guardian*, on August 1, 1997 (Attachment 30); a letter to the editor of a local newspaper, *the Georgia Guardian*, that was

published on August 8, 1997 (Attachment 31); a summary from a local television station, Channel 3, WSAV(NBC), disclosing details of the study that was broadcast on July 15, 1997 (Attachment 32); and a series of questions and answers that were available for use in response to any questions received regarding the study or the product (Attachment 33). In accordance with 21 CFR §312.54, this information is also being submitted to the IND file.

Based on information received from the clinical site, the investigator and IRB achieved community consultation by publishing an advertisement in the local newspaper (Attachment 29), and disclosing the study on a local television news broadcast (Attachment 32), both of which included a telephone number established for soliciting communication from the public.

Public disclosure from Richland Memorial Hospital included informing hospital personnel through various meetings, presentations, and administrative briefings; a notice that was faxed to hospital physicians and also posted in physician lounges (Attachment 34); a copy of an article that appeared in an employee newsletter, *Focus,* on July 3, 1997 (Attachment 35); a copy of the material presented at the Columbia Medical Society/Executive Committee Meeting, which was attended by chiefs of staff of other Columbia hospitals (Attachment 36); an article that was published in the June edition of *The Recorder,* a Columbia Medical Society publication, that included a summary of the study and provided a phone number for people to call with questions (Attachment 37); an informational letter and package containing a summary of the study, trauma statistics and information, and a question and answer sheet that was given out at the press conference, and also mailed to special interest groups, including minority leaders, business leaders, American Red Cross, EMS, Medical Directors of 17-County Emergency Rooms, USC Vice Chairman of Research, area Clergy, South Carolina Medical Association, DHEC EMS Division, SCOPA, and Columbia Police/Richland County Sheriff (Attachment 38); a copy of a news release that was given out at the press conference and also mailed to media who did not attend (Attachment 39); a copy of an article that was published in a local newspaper (Attachment 40); and copies of news clips that were published in local newspapers, *the Morning News,* and *The Post & Courier,* on July 9, 1997 (Attachment 41). Two local radio stations broadcasted interviews with the principal investigator; one local radio station provided an opportunity for listeners to call in with questions about the study protocol and product; three local television stations covered the press conference; the principal investigator met with elected officials and different key concerned citizens to discuss the study; and information about the study, as well as a copy of the question and answer sheet (part of Attachment 38) was distributed to participants in the Columbia Medical Society mini-internship program. Finally, at the press conference, the principal investigator presented the research, it's benefits to the community, and local demographics, morbidity, and mortality statistics in the study patient population. In accordance with 21 CFR §312.54, this information is also being submitted to the IND file.

Based on information received from the clinical site, the investigator and IRB achieved community consultation by providing a package containing study information to various groups with contacts for additional information and inviting them to a press conference (Attachment 38); having face to

face meetings with elected officials and other key community members; broadcasting interviews with the principal investigator on local radio stations, which provided an opportunity for listeners to call in with questions about the study; and holding a press conference which various groups were invited including the news media where the study was presented and questions addressed. This press conference was attended by 38 people.

Additional information from Lehigh Valley Hospital includes an agenda from a meeting between the study investigators and the Hospital Liaison Committee for Jehovah's Witnesses (Attachment 42). In accordance with 21 CFR §312.54, this information is also being submitted to the IND file.

The submission has been organized as follows:

R.A. Cowley Shock Trauma Center

- Attachment 1: Agenda for a community meeting
- Attachment 2: Minutes from the community meeting
- Attachment 3: Handout provided at the community meeting
- Attachment 4: Article that appeared in a local newspaper
- Attachment 5: Transcript from a local television broadcast
- Attachment 6: Transcript from a local television broadcast
- Attachment 7: A letter to the Editor of a local newspaper
- Attachment 8: Transcript from a local television broadcast
- Attachment 9: Press Release
- Attachment 10: Advertisement that appeared in a local newspaper
- Attachment 11: Advertisement that appeared in a local newspaper

Allegheny University of the Health Sciences

- Attachment 12: Minutes from a Community Consultation Meeting
- Attachment 13: Transcript from Community Consultation Meeting
- Attachment 14: Minutes form a Community Consultation Meeting
- Attachment 15: Transcript from local radio program
- Attachment 16: An advertisement announcing Community Meetings
- Attachment 17: Transcript from April 11, 1997 Community Meeting
- Attachment 18: Transcript from April 16, 1997 Community Meeting
- Attachment 19: Transcript from April 17, 1997 Community Meeting
- Attachment 20: A letter sent to key community members
- Attachment 21: An article published in local newspapers
- Attachment 22: An article published in a local newspaper
- Attachment 23: An article published in the Hospital newspaper
- Attachment 24: An abstract submitted to the EAST Association
- Attachment 25: A public service announcement
- Attachment 26: List of radio and television stations that received the public service announcement

Memorial Medical Center, Inc.

- Attachment 27: Press release
- Attachment 28: List of surrounding hospitals that received press release
- Attachment 29: An advertisement published in a local newspaper and distributed as a flyer to the hospital staff
- Attachment 30: An article in a local newspaper
- Attachment 31: A letter to the editor of a local newspaper
- Attachment 32: Summary of a local television news broadcast
- Attachment 33: List of questions and answers regarding the study and the product

Richland Memorial Hospital

- Attachment 34: Notice that was faxed to hospital physicians and posted
- Attachment 35: An article that appeared in a hospital newsletter
- Attachment 36: A copy of the material presented at a Committee Meeting
- Attachment 37: An article that was published in a Columbia Medical Society publication
- Attachment 38: Informational letter and package that was given out at the press release and mailed to special interest groups
- Attachment 39: A news release
- Attachment 40: An article that was published in a local newspaper
- Attachment 41: News clips that were published in local newspapers

Lehigh Valley Hospital

- Attachment 42: Agenda from a meeting

If there are any questions concerning this information, please contact me at (847)270-5313.

Sincerely,

Rita Sichu for Maulik Nanavaty

Maulik Nanavaty, Ph.D.
Director Regulatory Affairs
Blood Substitutes Program

Attachment 1

000-000001

UNIVERSITY OF MARYLAND
SCHOOL OF MEDICINE

OFFICE OF THE DEAN
Office for Research Subjects

655 West Baltimore Street, Room 14-016, BRB
Baltimore, Maryland 21201-1559
Voice: 410 706-5037
Fax: 410 706-0189
Email: ORS@SCHMED01.AB.UMD.EDU

UNIVERSITY OF MARYLAND AT BALTIMORE
INSTITUTIONAL REVIEW BOARD (IRB)
COMMUNITY MEETING
AGENDA

April 9, 1997 - 7-8 p.m.
1010 W. Baltimore Street
Concerned Citizens of Poppleton

I. Welcome and Introduction — Rev. Robinson

II. UMAB-IRB Research Summary — Paul Fishman, M.D.

III. Question and Answer Period

IV. Emergency Research Study — David Gens, M.D.

V. Wrap Up Discussion/Question & Answer

Attachment 2

#0297114 PI: Dr. Gens
"THE EFFICACY TRIAL OF DIASPIRIN CROSS-LINKED HEMOGLOBIN (DCLHb-tm) IN THE TREATMENT OF SEVERE TRAUMATIC HEMORRHAGIC SHOCK"

COMMUNITY CONSULTATION MEETING MINUTES:

The Community Consultation meeting took place on Wednesday, April 9th. This meeting is in connection with the recently implemented FDA/OPRR regulations regarding waiver of informed consent for emergency research.

The meeting was hosted by the Board of Directors of 'Concerned Citizens for Poppleton' of which Rev. Robinson, the IRB Community Rep, is President. UMAB representation included Dr. Fishman, IRB Chair, Dr. Gens the Principal Investigator for the emergency research and IRB staff.

Dr Fishman provided an overview of UMAB, the IRB and research activities. Dr. Gens provided a detailed description of the emergency research, a new hemoglobin product for subjects presenting at Shock Trauma with severe blood loss.

There was consensus by meeting participants that the study was an important one and that the study should be conducted even if informed consent could not be obtained. Dr. Gens agreed to provide a copy of the public notice to the group for their information. Recommendation was made that the notice appear in the Baltimore Times and City Paper in addition to plans for the Baltimore Sun to ensure broader coverage of the public notice.

Dr. Gens will provide periodic updates of the status of the study regarding subjects enrolled, interim results and other relevant information.

The group requested that information regarding the demographics of shock trauma patients be made available to them on a periodic basis.

Additional issues raised during the meeting included the need for broader community representation on the IRB to ensure that 'community representation' is more inclusive. The group voiced concern that a need exists for dialogue of UMAB research activities in general so that they are knowledgeable about research activities that impact members of the community. Dr. Fishman acknowledged both of these areas and agreed to review and consider additional members to the IRB.

Attachment 3

EMERGENCY RESEARCH CONSENT WAIVER

WHAT: The FDA and HHS have combined efforts and finalized federal regulations allowing for waiver of informed consent for subjects in emergent circumstances such as trauma and head injury

WHEN: Effective November, 1996

WHY: Response to growing concerns that previous regulations, were making high quality research in emergency circumstances difficult or impossible and also prevented subjects from receiving the benefits of new therapies

HOW: Once the IRB has reviewed and approved the study design and determined that the research provides the prospect of direct benefit to subjects and that obtaining informed consent is not possible because

- subjects are in a life-threatening situation
- subjects are unconscious and cannot give their informed consent
- the intervention must be given before consent from family members can be obtained

WHAT ELSE: In exchange for the waiver of informed consent, additional protections of the rights and welfare of subjects must take place. They include

- Consultation with the community where research is taking place and from which the subjects will be drawn. For local community- arrange through the IRB. For a disease related community (cancer) local chapter of disease non-profit group (American Cancer Society) may be substituted with IRB approval.
- Public Disclosure of research progress and results, and
- Establishment of an independent data safety monitoring committee to exercise oversight

Attachment 4

SAT Apr 19, 1997 Section B

BALT. SUN Sect B

DOUG KAPUSTIN/SUN STAFF

...rmy Corps of Engineers, pauses during an observance and wreath-laying at the Fallon ...rday. The event was to mark the second anniversary of the Oklahoma City bombing on ...ere killed.

Hospital's experiment draws worry

Shock Trauma plans trial of new therapy without subjects' OK

FDA loosened its rules

Poppleton residents say facility should publicize test more

By MARILYN MCCRAVEN
SUN STAFF

Some gunshot and stabbing victims treated at Maryland Shock Trauma Center will become subjects in a medical experiment that some people say raises serious ethical issues.

The experiment begins next month and is expected to last six months, involve 25 patients and, doctors hope, save about three lives.

Selected patients will be given a blood substitute called HemAssist, which is made from human blood, apparently speeds life-giving oxygen to vital organs and raises blood pressure faster than traditional therapies of salt solutions and blood transfusions.

No time would be lost while blood-matching tests were done because HemAssist can be given to patients with any blood type.

By running the trial at Shock Trauma, the University of Maryland Medical Center will become the first local hospital to confront the ethical dilemmas of the U.S. Food and Drug Administration's decision last fall to partly lift a 50-year ban on involuntary medical testing on human subjects.

"This is the first time we will be permitted to do a research project at Shock Trauma without the patients' permission or their families' permission," said Dr. Paul Fishman, a professor of neurology and chairman of the university board that oversees medical research.

A spokeswoman for the Johns Hopkins University School of Medicine said researchers there will do human experimentation in the emergency room under the new rules, too, but they are still working on preliminary plans.

The change is restricted to federally approved experiments done on a limited number of patients who otherwise would likely die. A ban remains in effect for non-emergency testing.

Before entering patients in a trial, the hospital is required to attempt to reach their next of kin to obtain consent that patients are unable to give.

Even with such guidelines, some medical ethicists and others are wary of using unconscious patients in tests of experimental treatments after the patients are wheeled into emergency rooms.

Dr. Arthur L. Caplan, a medical ethicist at the University of Pennsylvania, criticizes the regulations as "too broadly written and too vague. ... This is not adequate regulation for this sensitive and [See Shock, 4a]

Parole panel's chief is replaced

Patricia Cushwa, 58, advocate of victims, to lead Md. commission

By THOMAS W. WALDRON
SUN STAFF

Gov. Parris N. Glendening replaced the longtime head of the Maryland Parole Commission yesterday with Patricia K. Cushwa, an advocate for victims' rights and a member of the parole panel since 1992.

Cushwa, 58, will succeed Paul J. Davis, who has been chairman of the eight-member commission since 1988 but was not reappointed by Glendening at the expiration of his term in December.

Cushwa, who helped start a victims' advocacy group in her Washington County home 20 years ago, said her appointment is a "strong signal that victims matter."

"This is an opportunity to look at ourselves with a ...

...or not? big flap

...t thing that has happened to St. Michaels since ...British bombed it," said ...Cowee, the Talbot ...ty planning officer, re...ing to the shelling of the ...n by English warships ...fty two centuries ago.

...st issue is the future of St. ...haels, the self-described ...el of the Eastern Shore." ...wn has a population of ...ut 1,300 and attracts ...000 or so other people ev...ear.

...local landowner's re...t that the town annex ...acres on its eastern ...ndary on which 250 ...es and some commercial ...ings would be built has ...ed up such a controversy ...the landowner has tem...rily withdrawn the plan ...at he can prepare it for ...ected legal action by the ...mission.

Opponent: *Deborah Bridges says the proposed development, which would be across from her shop, is "sickening."*

Supporters of the proposal say it is the best way to manage inevitable growth. Opponents say it would destroy a unique charm and cachet that have been 300 years in the making.

Local opposition to growth isn't new — two requests [See St. Michaels, 4a]

AMY DAVIS/SUN STAFF PHOTOS

Owner: *Clint Wadsworth, who wants St. Michaels to annex his Hatton's Garden property along San Domingo Creek, says his development proposal would enhance the town. "The time is right to plan it for the next 20 to 25 years," he says.*

Best store tilted wall tumbles down

Towson landmark goes in center renovation

By SUZANNE LOUDERMILK
SUN STAFF

The landmark tilted wall came tumbling down yesterday in the blink of an eye, turning 450 tons of steel and concrete into a giant scrap heap.

After almost 20 years, the unusual Best Products store at Towson Marketplace was demolished by cranes to make way for a Target store, part of a $20 million renovation of the shopping center.

Its demise brought dozens of area residents and workers to the dust-swept parking lot at Putty Hill Avenue and Goucher Boulevard to watch the unusual architecture crumble. By 10 a.m., they had lined up their cars like patrons at a drive-in theater waiting for the show to begin.

"I've been coming to the mall since I was a little kid," said Abe Schroen, 18, of Parkville, sitting on the hood of his car. "It's like the last piece is coming down."

The distinctive Best facade that [See Best, 2a]

the giant squid

Dead n...

ock Trauma experiment drawing concern

(Shock, from Page 1B)

troubling kind of work."

Caplan is particularly concerned that the revised FDA regulations are vague concerning public notification.

The regulations allow public announcement, even newspaper advertisements, to substitute for informed consent — the principle of asking prospective participants if they want to be part of a medical experiment and fully informing them of the risks and benefits before they enroll.

The difficulty in giving adequate public notification was obvious April 9, when Fishman and Dr. David Gens, an assistant professor and a surgeon at Shock Trauma, met with residents of the Poppleton neighborhood in southwest Baltimore to announce the new regulations.

The doctors said the university had determined that Poppleton, which is across Martin Luther King Jr. Boulevard from the university medical complex, was the hospital's "community" in terms of satisfying the federal requirement for notification. They also said an advertisement spelling out the rules change would run in *The Sun*.

"This is the only community group we know," Fishman told community representatives in response to a question about why other community groups hadn't been contacted.

Several of the dozen or so people attending the meeting of Concerned Citizens of Poppleton said Shock Trauma officials need to go greater lengths to notify the broader community, including addressing other community groups, running ads in free newspapers that more poor people would read and adding people from the community to the board that governs university medical research.

Gens said public notification was a key subject at two meetings of some 40 major medical centers where the FDA rules were discussed.

"At one of those meetings, I said, 'I'm from the Shock Trauma Center in Baltimore. What is my community? We receive patients from all the different counties in Maryland, even from Delaware, West Virginia and Pennsylvania. Do I have to go to every community in all these states?'

"The answer was, 'No, you don't. You should go to communities that are closest to your hospital that your [board that oversees research] feels you should.'"

For the mostly African-American audience at the Poppleton meeting, involuntary medical testing raised the specter of the notorious Tuskegee Study, in which public health officials, starting in the 1930s, did not tell poor, black Alabama men they had syphilis and withheld a cure when it was discovered.

"When you're talking about shootings and stabbings, you're talking about young black males, and we'd like to know how many of them will be affected by this," said the Rev. Edward G. Robinson, president of the Poppleton group.

Fishman and Gens tried to allay group members' fears, assuring them that only treatments already proved safe in human testing will be used. No children or pregnant women will be included.

Fishman said the university will seek public comment on any human experimentation done under the FDA's new rules. If the community opposes a specific experiment, "we'd have to rethink it ... maybe change the study."

Caplan, the medical ethicist, said that instead of lifting the ban, the government should have considered issuing cards similar to organ donor cards to people who wish to receive experimental treatments in the event of catastrophic illness or injury.

Fishman said such moves historically have not proved practical because few people will sign up to be research subjects in the event they need emergency treatment.

Medical researchers say the ban on human experimentation without informed consent slowed development of therapies that could help victims of heart attacks, strokes and traumatic injuries.

The FDA said it tried to balance patients' rights with the need for new medical technologies. "The rules are put together in ... an ethically sound way," said Donald C. McLearn, a FDA spokesman.

Five hospitals nationwide are preparing to be the first to use HemAssist, the blood substitute produced by Baxter International Inc., in this phase of clinical trials. It's the final phase before FDA approval. The drug is expected to become available nationally next year.

HemAssist has been tested on 700 people. It is primarily hemoglobin, the protein that gives blood its color and carries oxygen through the bloodstream.

Side effects include stomach cramps, a temporary yellowing of the skin and a red tinge to the urine, which occur as the hemoglobin molecules break down.

Said Gens, "We really believe we can save more lives using this new therapy."

...didn't think the develope... his concern for growth co... with preserving St. Mich... proposal for townhouses ... gle-family residences, ca... lower density than is p... under current county zon... homes per acre compare... per acre — and he said h... development that would ... the town.

"The time is right to pl... the next 20 to 25 yea... Wadsworth, who grew up ... ton's Garden Farm and ... nearby Royal Oak. "W... been concerned about is... these controls set even b... start talking to developer... have controls."

Careful management ... velopment could bring be... the town, said Wadswo... envisions a public park ... property and houses tha... enhance, not damage, ... chaels' ambience.

Opponents see it dif... "It's sickening," said ... Bridges, owner of Swa... Flowers, Antiques and ... ibles, a St. Michaels shop... boils down to pure greed ... ing to kill this town."

"The town historically ... percent growth — it wa... like. Die, move out and w... in someone to replace yo... Robert E. Hofmaster, a r... dent who is leading the ... chaels Preservation Coalit...

"There are two main ... St. Michaels might want ... that land," Bird said. "We ... trol how it is developed ... don't annex it, developm... be controlled by the coun... would generate additiona... ty taxes, which the town n...

St. Michaels probabl... benefit from the develop... Hatton's Garden, said ... Smith, a town commissi... town treasurer. It wou... growth the town needs, a... tax revenues, he said.

Attachment 4 Con't.

The Baltimore Sun

April 19, 1997, Saturday, FINAL EDITION
SECTION: LOCAL (NEWS), Pg. 1B

LENGTH: 1129 words

HEADLINE: Hospital's experiment draws worry; Shock Trauma plans trial of new therapy without subjects' OK; FDA loosened its rules; Poppleton residents say facility should publicize test more

BYLINE: Marilyn McCraven, SUN STAFF

BODY:

Some gunshot and stabbing victims treated at Maryland Shock Trauma Center will become subjects in a medical experiment that some people say raises serious ethical issues.

The experiment begins next month and is expected to last six months, involve 25 patients and, doctors hope, save about three lives.

Selected patients will be given a blood substitute called HemAssist, which is made from human blood, apparently speeds life-giving oxygen to vital organs and raises blood pressure faster than traditional therapies of salt solutions and blood transfusions.

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"This is the first time we will be permitted to do a research project at Shock Trauma without the patients' permission or their families' permission," said Dr. Paul Fishman, a professor of neurology and chairman of the university board that oversees medical research.

A spokeswoman for the Johns Hopkins University School of Medicine said researchers there will do human experimentation in the emergency room under the new rules, too, but they are still working on preliminary plans.

The change is restricted to federally approved experiments done on a limited number of patients who otherwise would likely die. A ban remains in effect for non-emer-gen-cy testing.

Before entering patients in a trial, the hospital is required to attempt to reach their next of kin to obtain consent that patients are unable to give.

Even with such guidelines, some medical ethicists and others are wary of using unconscious patients in tests of experimental treatments after the patients are wheeled into emergency rooms.

Dr. Arthur L. Caplan, a medical ethicist at the University of Pennsylvania, criticizes the regulations as "too broadly written and too vague. This is not adequate regulation for this sensitive and troubling kind of work."

Caplan is particularly concerned that the revised FDA regulations are vague concerning public notification.

The regulations allow public announcement, even newspaper advertisements, to substitute for informed consent -- the principle of asking prospective participants if they want to be part of a medical experiment and fully informing them of the risks and benefits before they enroll.

The difficulty in giving adequate public notification was obvious April 9, when Fishman and Dr. David Gens, an assistant professor and a surgeon at Shock Trauma, met with residents of the Poppleton neighborhood in Southwest Baltimore to announce the new regulations.

The doctors said the university had determined that Poppleton, which is across Martin Luther King Jr. Boulevard from the university's medical complex, was the hospital's "community" in terms of meeting the federal requirement for notification. They also said an advertisement spelling out the rules change would run in The Sun.

"This is the only community group we know," Fishman told community representatives in response to a question about why other community groups hadn't been contacted.

Several of the dozen or so people attending the meeting of Concerned Citizens of Poppleton said Shock Trauma officials need to go to greater lengths to notify the broader community, including addressing other community groups, running ads in free newspapers that more poor people would read and adding people from the community to the board that governs university medical research.

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Side effects include stomach cramps, a temporary yellowing of the skin and a red tinge to the urine, which occur as the hemoglobin molecules break down.

Said Gens, "We really believe we can save more lives using this new therapy."

Pub Date: 4/18/97

LOAD-DATE: April 21, 1997

VMS
VIDEO MONITORING SERVICES OF AMERICA, L.P.

New York (212) 730-2010
Los Angeles (818) 953-0111
Chicago (312) 649-1131
Philadelphia (215) 592-8080
San Francisco (415) 543-3567
Detroit (810) 352-0330
Boston (617) 262-2121
Dallas (214) 844-0006
Houston (713) 780-1825
Miami (305) 576-8541
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Hartford (860) 236-6697
San Diego (619) 544-1880

5000 National Press Building
Washington, DC 20045
(202) 783-7110
(202) 393-5451

Transcript

DATE April 19, 1997
TIME 9:00-9:30 AM
STATION WBAL-TV(NBC) Channel Eleven
LOCATION Baltimore
PROGRAM 11 News Saturday Morning

Dina Napoli, co-anchor:

A planned experiment at shock trauma is causing some concern this morning. According to a report this morning in the Baltimore Sun about two dozen patients suffering from gunshot wounds or stab wounds will become part of an experiment to test a blood replacement item called hemocyst (sp), which experts say will help save lives. The test comes after the Food and Drug Administration partially lifted a ban on involuntary human testing.

# # #

Attachment 6

VIDEO MONITORING SERVICES OF AMERICA, L.P.

New York (212) 736-3010
Los Angeles (213) 883-0111
Chicago (312) 648-1131
Philadelphia (610) 668-4008
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Hartford (860) 236-4422
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3000 National Press Building
Washington, DC 20045
(202) 383-7110
(202) 383-5451

000 - 0000

Transcript

DATE April 19, 1997
TIME 10:00-10:30 PM
STATION WBFF-TV(FOX) Channel 45
LOCATION Baltimore
PROGRAM Fox 45 News at Ten

Jennifer Gilbert, co-anchor:

An experiment scheduled to begin next month at Shock Trauma in Baltimore has sparked some ethical questions. The experiment involves giving gunshot and stabbing victims a blood substitute called hemocyst (sp). It's made from human blood, but it's compatible with all blood types. The debate is whether patients who likely will be unconscious, should be given the blood substitute without their consent.

# # #

Attachment 7

The Baltimore Sun

May 2, 1997, Friday, FINAL EDITION
SECTION: EDITORIAL, Pg. 12A, LETTERS

LENGTH: 1128 words

Patients shouldn't be tested without consent

The April 19 edition of The Sun described a six-month trial to be run at the Shock Trauma Center at the University of Maryland Medical Center. Doctors will use a blood substitute, HemAssist, on selected patients without their consent if they cannot communicate and next of kin cannot be located before the blood is needed.

Proving the use of the blood substitutes to improve emergency treatment is a worthy project. However, the treatment of patients for clinical trials without their consent or knowledge crosses an ethical line.

It seems not enough thought has been given to the importance of patients' rights and possible alternative ways to prove the use of this blood substitute with the permission of the patient.

I am amazed, considering the historic abuses of government experiments without the knowledge of the person being tested, that the government would allow a newspaper ad and a discussion with one small community to substitute for patient consent.

Even if notification of next of kin to get consent means the experiment will take much longer than the expected six months, this is the price we must pay to preserve the right of the patient.

Charles Culbertson
Towson

Attachment 8

VIDEO MONITORING SERVICES OF AMERICA, L.P.

1666 National Press Building
Washington, DC 20045
(202) 383-7110
(202) 383-5451

New York (212) 736-2010 | Los Angeles (213) 993-0111 | Chicago (312) 649-1131 | Philadelphia (215) 569-4990 | San Francisco (415) 543-3361
Detroit (810) 352-9220 | Boston (617) 266-2121 | Dallas (214) 644-9696 | Houston (713) 789-1636 | Miami (305) 576-3591
Denver (303) 733-8000 | Hartford (860) 236-6662 | San Diego (619) 544-1880

Transcript

DATE May 2, 1997
TIME 6:00-7:00 PM
STATION WJZ-TV(CBS) Channel Thirteen
LOCATION Baltimore
PROGRAM Eyewitness News

Vic Carter, co-anchor:

If you were injured in an accident and needed blood, would you want the real thing or a new blood substitute? It's being tested right here in Baltimore. We'll have the story next in Health Watch.

* * * * * *

Carter: Fake blood is what makes horror movies so lifelike, but fake blood will soon be used in real life in hospitals, one of them right here in Baltimore.

Health Watch reporter Kellye Lynn is here now with details.

Kellye Lynn reporting:

This month Shock Trauma is going to test artificial blood products on ER patients, Vic. In tonight's Health Watch, Shock Trauma is one of the hospitals nationwide to test the fake blood called Hemassist. Some doctors say its the blood of the future. But critics say there's too much excitement and not enough facts known about it.

Kai Jackson explains the controversy.

Kai Jackson reporting:

Car accidents, shootings, and stabbings. Different kinds of trauma cases with one thing in common: the victims need blood.

Dr. Paul Fishman (Hospital Ethics Board): And trauma victims were bleeding to death because we have to get them oxygen to their brain and to the heart as quickly as possible.

Jackson: And that can mean the difference between life and death. So starting this month at Shock Trauma, doctors will give select emergency patients a new blood called Hemassist. Scientists say it works faster than

regular blood.

Fishman: It's basically a hemoglobin solution- human hemoglobin solution which has been stabilized so it does its job, so that it delivers oxygen to the tissues.

Jackson: Hemassist is a manufactured human blood. After years of research, scientists were able to extract the richly desired hemoglobin from the blood and eliminate the need for different blood types. And now there's FDA approval to conduct an experiment with it.

Dr. David Gens (Shock Trauma): The best medical therapy that we currently can provide them, many of them will still die, will bleed to death and die.

Alfred Boyd (Concerned Citizen): I read the article that- how it would affect Baltimore city citizens.

Jackson: Doctors are quick to point out what Hemassist is and does, but Alfred Boyd says he wishes patients who'll get it knew the same.

Boyd: Hemassist, again, I don't know what it is. It could be tainted. Who knows? It could be- it could be anything. Who knows?

Fishman: It has been treated so that there is no possibility of virus particles such as the AIDS virus or hepatitis viruses.

Jackson: Under the experiment, doctors are required to seek consent to use Hemassist on patients. But if they can't get it and a life is in danger, the FDA allows doctors to give the blood anyway. So does that make the unsuspecting patients guinea pigs?

Reverend Edward Robinson (Hospital Ethics Board): In clinical trials such as these, when seven hundred people have already taken the medication, I wouldn't say that the recipient would be a guinea pig. No, sir, I wouldn't feel that way at all.

Jackson: It remains to be seen whether Hemassist will prove to be a wonderblood. But there are those who believe not enough is known about this new product. Now doctors cringe at the thought of Hemassist being compared to the notorious Tuskegee experiments. But while the Tuskegee history is being reviewed, there are those who believe that the introduction of Hemassist now is at best awkward.

What concerns some is so many African Americans are the victims of violence in Baltimore, and those victims may end up at Shock Trauma, and may be more likely to get Hemassist.

Robinson: I think the timing for this research is not particularly good. I think that's why it's under a lot of scrutiny, and I certainly wouldn't want to see anything such as what happened in Tuskegee happen here.

Gens: The whole reason to provide them, the whole reason that we're doing the research is to improve their likelihood of survival, not to diminish it.

Sister Margaret Downing (Concerned Citizen): We'll be watching this as a community very carefully to see whether this is- has some positive effects, the kind of positive effects that they are saying to us will be coming forth.

Jackson: Kai Jackson, Channel 13, Eyewitness News.

Lynn: And the FDA is closely monitoring the Hemassist trials. Findings will be available later.

Carter: Let's assume for discussion's sake that this does become very popular and it is used quite a bit. Does this mean that we will no longer need to go and donate blood?

Lynn: Well, according to Kai, no. He says that doctors say it will not decrease the need for people to donate blood.

Carter: Okay, thank you.

# # #

Attachment 9

Press release
Baltimore Sun, Baltimore Times, City Paper, and The Afro-American.

R A. Cowley Shock Trauma Center
Studies New Hemoglobin Product for Severe Blood Loss

The R A. Cowley Shock Trauma center is one of approximately 40 sites throughout the United States asked to test a new blood substitute on patients with severe blood loss (hemorrhagic shock.) This hemoglobin solution, known as Diaspirin Cross-Linked Hemoglobin (DCLHb™), has been developed by Baxter Healthcare, Inc. and has the potential to treat and prevent the harmful side-effects of severe blood loss. These side effects include low blood pressure, severe illness or death.

The U.S. Food and Drug Administration (FDA) has recently developed a set of guidelines for emergency research, in which patients are unable to give permission to participate. Due to the fact that traumatic accidents are sudden and unexpected, and after careful consideration of past research involving DCLHb™, the FDA has ruled that this study conforms to the strict guidelines for exception from informed consent. Along with strict regulations for the implementation of this study, the FDA requires that the public be informed about this product before the study commences. To communicate with us on this topic, please contact:

David R. Gens, MD
R A. Cowley Shock Trauma Center
Program of Trauma
22 S. Greene Street
Baltimore, MD 21201
(410) 328-3055

For further information about rules regulating research with human subjects, contact the Institutional Review Board (IRB) at (410) 706-5037.

First African-American female

[illegible] High Sch[illegible]

Nominees for two at-large positions must be selected by parent and community groups. Nominations must be submitted by June 13 to the New Board of School Commissioners, 200 E. North Avenue, Room 406, Baltimore, MD 21202. On June 18, the nominees will be presented to

serve for two years and may not serve more than two consecutive terms.

To be successful, the New Board must have active, consistent, and continual parental involvement. The role of the PCAB is critical in ensuring that the New Board and CEO

Young

By Delarita C

Muscles tighten, blo pressures rises, the heart spe up, extra adreneline ru through your system. If sounds familiar, you may h experienced STRESS. Stress automatic physical reaction danger or demand.

Stress is a fact of life some stress can be good fo because it inspires you to meet life's challenges. Bu much stress can harm physical and mental well-b That's why you need to be a control stress - so that it doe control you.

Naturally, no one remedy reduce stress for everyone, so first step is to find out w method works for you. You develop a Personal Manage Stress Program.

Pressure and demands on energy and time can come f every corner in your life. Bu sources of stress are norm found: At Your place Employment, in your personal and in your environment.

Regardless of the source, system to reduce stress systematic:

Do something YOU enjoy. aside time for yourself. You time for relaxation and recrea - take time-outs regularly. D with commitment! Nearly ev stress reducing activity immediate results. It is impor to stick with the activity.

Given the challenges engulf the work place today, important to be able to recog symptoms of stress. You

personal tragedy, t problems arise, or health the worst. All of the potential signs that you ar profile. Too many to activities in a one to t period, increases your cha

According to research, the U.S. over $200 billio in stress-related absen lowered productivity, ir medical compensation, a direct related claims. But more strategies to assist managing stress:

Start the day off wit lights - it energizes your b

Find a laugh - Laught starts you body, and endorphins;

(Italics) , Stretch yours this activity will increas flow;

Focus on exhaling breaths relaxes you;

Bath - Take one "I Bath."

In our seminar, Ma Stress to Success, w exercises that increase th flow, and exercises to c down. It is a great experie a great means to learn control your body. Li what's going on inside yo its the only one you have.

Karen and Lorinzo F are partners at Synectics T They teach semina Interpersonal Developm specialize in "upsk employees.

Synectics Trainers, 452. Owings Mills, Md 21117.

RA Cowley Shock Trauma Center Studies New Hemoglobin Product for Severe Blood Loss

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David R. Gens, M.D.
RA Cowley Shock Trauma Center
Program of Trauma
22 S. Greene Street
Baltimore, MD 21201
(410) 328-3055

For further information about rules regulating research with human subjects, contact the University of Maryland Institutional Reviews Board (IRB) at (410) 706-5037.

Attachment 11

PUBLIC NOTICE

RA Cowley Shock Trauma Center Studies New Hemoglobin Product for Severe Blood Loss

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Program of Trauma
22 S. Green Street
Baltimore, MD 21201
(410) 328-3055

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Attachment 12

Community Consultation Meeting
March 7, 1997
Minutes

Thomas A. Santora, M.D.
Ruthann Dailey
Leah Rapposelli
B.J. Moore, R.N.
Sally Hilton
Serita Reels
Mr. Darryl Davenport
Officer Velma Dean
Pastor William Marquand deHeyman
Dr. Jesse Gardner
Reverend Florence Gelo
Ms. Roberta Ginsberg
Mr. Billy Sconniers
Reverend Thomas Sligh
Mr. Le Roi Simmons
Mr. Charles Whiting

1. Presentation

The problem encountered by severely traumatized patient was introduced. The potential beneficial aspects of DCLHb were reviewed along with the need to apply the new FDA's exception to informed consent for this study protocol.

2. Community Issues

In general, community members voiced an overall "suspicion." Though they are in favor of being on the cutting edge of potentially beneficially therapy for this population of trauma patients, they felt additional communication would be needed to alleviate their basic feeling of suspicion. These suspicions specifically were as follows:

a. The community now views Allegheny University Hospitals as "big business" - suspicious as to why this big business is now interested in their community.

- Reviewed previous outreach projects.
- Acknowledged that community activities should have been greater in the past.

b. Will race, creed and especially color dictate who is enrolled in this study?

- The entry criteria for the study was reviewed.
- The process of randomization once entry criteria have been met was outlined. The concept that the research investigator was not able to control who received or did not receive study material was well received.

c. Can the hospital overcome some of the negative impressions made to the community due to less than efficient care provided in the past? Examples cited were long delays in the Emergency Center as well as the outpatient clinics. There was perception that the underprivileged or minority patient population have been treated in a substandard fashion.

- Acknowledged that we have work to do to improve all "service areas," regardless of race, color, creed or economic status of our patients.

d. Will the minorities be treated differently or bare the bulk of the experimentation in this research trial such as was done in the past, especially noting that Tuskegee experience. The community voiced clearly their suspicion of the federal government.

- I outlined the federal guidelines and indicated that in 1997, the federal government could never repeat the mistake they had done in the past with the Tuskegee experience. This is largely due to efforts by community spokespersons (like our community consultation members) who would not allow that discrimination to occur.

e. The question of remuneration for this study was raised.

- I shared with the community that remuneration was to the research program in the Division of Trauma to help fund additional research to promote further advances in trauma care. No personal financial benefits would be realized.

f. The community voiced suspicion about financial benefit achieved by the sponsor, Baxter Healthcare. They questioned the ownership of this company.

- Acknowledged that the sponsor hopes to bring this drug to market (where profits will undoubtedly occur).

g. Concern was raised that the investigators would not truly represent the community at large. The overall sentiment was that an individual of color would be well received if supporting this research project. This counsel strongly emphasized the importance of involving physicians of color.

- Acknowledged and planned for subsequent meetings.

Attachment 13

Community Meeting - March 7, 1997

My name is Thom Santora and I am one of the general surgeons in the hospital who has dedicated my area of interest to the care of the severely injured patients. The reason that we have asked you to come to talk with us today is to investigate your feelings about what I think is a great opportunity to improve the care of our injured fellow community members. What I would like to do is to go to a very short presentation of an investigative study that we had the unique opportunity to participate in and then get some feedback from the entire group and get a feel for where we need to go.

Specifically what we want to discuss today is our intention to do a research study that involves the use of a blood substitute for the treatment of patients that are severely injured. We need to really talk about the issue that surrounds using this type of intervention in this population of patients. Because of the injured type of patient population represents a unique challenge to informed consent I suspect that the conversation that we have is not going to be so much about this drug per se but the whole concept of informed consent. What I would like to do in that regard is to review some new federal guidelines that allow us to investigate potential exception to informed consent.

Person talks I cannot hear what she is saying

The drug that we are going to be looking out is called Diaspirin ???. It is made from red blood cells that have expired in a sense that when you give a unit of blood it can only sit on the shelf somewhere between 35-42 days. For whatever reason the Red Cross or Blood Bank does not have a need for that blood unit after that time it has to be either given to a research laboratory or disposed of. So what this drug is that it is made from those red

blood cells [illegible]

has done is broken the red blood cell covering or coating of the red cells and exposed the molecules hemoglobin that actually carries oxygen. What we want to do is to look at the use of this drug in patients that have severe trauma.

Why do we want to do research in this injured population? One-hundred forty thousand (140,000) Americans die every year as a result of trauma. Most of these patients die from hemorrhage and when the bleeding is so severe that it creates low blood pressure or hypotension the standard therapy that we practice in every hospital across the country in 1997 is associated with a 40% death rate in that particular patient population. So that in our estimation as health care providers is less than optimal and what we want to do is to study new interventions and new drugs that can be applied to this severely injured patient population to try and improve the outcome.

Q: Is the death rate of 40% because of bleeding or is it that it combines the percentage with other reasons for death?

A: The bleeding creates scenario where the organs do not get enough nutrients supplied and as such they begin to fail. So people die of head injury for example that clearly is encompassed into this 140,000 thousand patient population of people who die, but of the people who come bleeding and with a low pressure 40% of those people die because of the bleeding.

Q: Do these people who die so so after resuscitation?

A: They have not had a timely enough of intervention that the intervention has not been adequate for whatever reason.

Q: If it is not a timely enough intervention if it were a timely intervention using the current form of intervention would that decrease the 40%.

A: Intuitively you would think it would but unfortunately despite the fact that our paramedics and our EMS systems have developed tremendously since the injured patients are arriving in our emergency centers much faster then they ever have this death rate seems to continue to occur. It may be that a good portion of those patients that would have come in for low blood pressures if they would have languished out in the field for a longer period of time are now coming in better shape and have survived. Nonetheless, we still have a fairly consistent death rate from trauma and most of those deaths are related to the consequence of bleeding even though the EMS service has in fact improved considerably.

Q: How has the emergency room service improved? We use to frequently hear horror stories when the patient was lying out in the hall for hours without any care.

A: Well again, I think that in general patients that present with significant injuries are cared in a timely fashion in most emergency centers. Now, of course, there is exceptions to every rule but I do not think those exceptions influence these numbers to any appreciable degree.

What we need to do is to try and develop a strategy where we can use new interventions which have shown promise in animal studies and in prior studies that may have been done in Europe and apply them to this patient population. I feel that we should do a better job with this patient population then we are doing presently and though the interventions that we talk about today are not like interventions of Penicillin back in the 1940's that can reduce the mortality considerably. What we are really talking about is reducing this mortality maybe from 40% to 30%. You might say on the surface that does not sound like a lot but in fact with 140,000 Americans dying each year as a result of that if we can save an additional 10% we are talking about 35,000. As a whole for society these things would

add up considerably.

Q:(Thom) Why do we want to do a blood substitute study?

A:(Thom) With the numbers that I presented the current therapy with rapidly establishing Ivs, giving patients salt water and blood transfusions we have mortalities that we just described. In early operations we do not seek to influence that appreciably. This month is Red Cross month and it has been up and down with our blood supply. Right now we are not so bad but in general we can always use more red blood cells. This type of therapy if we could show that it has a benefit it might reduce our overall need for red blood cells. The trauma patient population uses 3,000,000 units of blood red cells each year. It is a tremendous burden on our Red Cross that is above and beyond the requirements for blood for routine operations. If we can find a drug that can reduce that need we can tremendously improve the overall health care system. Our purpose is to stabilize the patient from shock. Presently we do that by trying to give crystalloid fluids or salt water, blood transfusion and then early operation. What this drug will do is to potentially reduce an amount of blood that we need to stabilize these patients. Every patient in this study whether they receive the medication or otherwise will receive benefit just by the mere fact that we will be watching these patients more closely in terms of laboratory studies and how they respond to treatment in general. If we can demonstrate that this drug has beneficial effect when we incorporate that into standard practice we may be able to save the lives of many trauma patients.

Q:(Thom) Who can be enrolled in this study?

A:(Thom) Any male or non-pregnant female over the age 18. You might say why are we saying non-pregnant female. Because this medication has not been studied and its effects on the fetus have not been studied so we want to make certain that we do not do anything

bad to our unborn children. We need to make certain that these patients have shock. Shock means low blood pressure or the effects of low blood pressure and then they have to have those findings due to bleeding. That bleeding can be either externally or internal bleeding.

The study protocol is rather simple in and of itself. The study medication is as I described to you. All patients will get standard treatment whether that be operation, transfusion or just the salt water solution. Whatever is necessary to try and stabilize them. In addition, about 1/2 of the patients will receive the study drug. All patients will be watched for 28 days to see the effect of their injury on their outcome in terms of how well their organs are functioning and ultimately whether or not they live or die.

To reiterate DCLHB or Diaspirin ?? hemoglobin is a blood substitute. It is made from red blood cells that have no longer the capability of being used safely in a transfusion. The drug is made by breaking the coating of the red blood cells and then cross-linking or prelimerizing the medicine, the hemoglobin, just so that it is stable in solution. The interesting thing is that this medication carries oxygen as efficiently as our own red blood cells do. The beneficial effect of this medication is not only because it carries oxygen but it appears to normalize the blood flow to injured organs. Thereby it improves the most important nutrient delivery oxygen to cells to try and decrease the effects of injury. In the process of making this medication it is heated, filtered, pasteurized such that this reduces and eliminates the potential for viral transmission. That is above and beyond the studies that are done at the time that the blood is donated which as you all know they do a HIV test and all of the viral tests to try and minimize that potential, however, there is still a small chance that there may be virus in that blood but this pasteurizing process should

eliminate that risk.

The potential effects of DCLHB is that it has been shown in animal studies and in preliminary human studies that it universally increases blood pressure and for our trauma patients that is a tremendously beneficial effect because the population that we have targeted for this study are those that present with evidence of low blood pressure. This medication will do that. It increases the supply of oxygen to the cells and normalizes the flow of this important nutrient to the organs to try and minimize the effects of injury. In a study in heart surgery patients this drug has demonstrated a reduction in the transfusion requirements so that ultimately we may be able to stabilize these patients and reduce the overall blood transfusion requirements even though the procedure these patient will get blood transfusions if the doctor states that they need to have blood transfusions. Study medication does not preclude blood transfusion. The interesting thing is that because of the coating of the red blood cell is removed in this process that coating is what is important in the blood typing. Anyone can receive this medication. There will not be a blood reaction to this medication because the reaction that occurs occurs because of the coating on the blood cells but since that coating does not exist this can be used in any patient.

There are some downsides as there always is to anything. This medication will discolor the skin and it will usually do that for a transient period of time though shortly after the introduction of the medication to about five days. The appearance would be that of jaundice but when we look at the effects of jaundice it is usually do to an abnormality of the liver. Actually the liver of these patients or animals were normal and there was not any evidence from a laboratory standpoint that there was a problem with the liver and the yellow discoloration is because the mediation is actually in the skin for a transient period

of time. The medication when it comes out of the bottle is red and occasionally it is filtered by the kidneys and will turn the urine red. Again, that is a transient effect and has not been problematic.

Q:(Thom) Is this research safe? Because that is a key component to the real issue at hand. The entire protocol that I have summarized for you has been reviewed and approved by the US Federal Drug Administration and they have given their okay. In the process they look specifically at who is going to receive the medication, what the benefits to that patient population is and most importantly what is the risks of this medication. In weighing all of those the FDA sees this protocol as being beneficial and not risky.

DCLHB in the study medication has been used extensively for four years. The benefits that I demonstrated to you are from those animal and human studies. It has been reviewed in those human studies by hospital review boards that like the FDA have found the use of the drug in the populations that it was used in the benefit outweighed the risk. Independent experts and a safety monitoring board will be set up for this particular trial so that every patient enrolled there results go this agency, a panel of experts that do nothing more then look at the results of the study to see if the medication is having any untoward effects. If it is they will shut down the trial. Likewise, if the study shows that the medication is overwhelmingly beneficial, they will stop the trial as well and recommend to the FDA that this medication does not need to be studied any further but can be approved because it has been shown beneficial. With all of these reviews the process has been shown to have increased beneficial effects when compared to the risks.

To try and safe guard the community and the patient we have an institutional review board. It is called an IRB. It is a panel of scientists and lay people that look at each and every

research study that is done in this institution and this board has reviewed our study protocol and like the FDA before them have agreed that the benefits for this patient population far outweigh the potential risks of the study. The research has been fully approved by the federal government and the real issue at hand is the new guidelines by which we are allowed to do this study. The medication is worth it. The real issue at hand here is that the people we are trying to treat are so severely injured that they will not be able to participate in the informed consent process.

Q: Is Baxter ?? asking you to do this research?

A: Yes they are

Q: Are we the only hospital doing this research?

A: This is a multi-center trial that is going to be going on across the country. The only approved site thus far has been in Allentown, Pennsylvania at the Lehigh Valley Hospital but the next couple of centers that bring this ?? will be done in Delaware and Washington DC but the studies centers are all over the country.

Q: Are you paid to do this study?

A: We get compensated in a reasonable fashion for what we do which goes into our ability to do other research projects. So no one, like myself, I do not benefit personally.

Q: The hospital benefits?

A: Correct. The hospital and research programs benefits so that we can continue to investigate new treatments for the care of injured patients. In my particular area of expertise that is what I do. I do not gain any personal benefit out of being involved in this study.

The specific criteria for this new exception to informed consent. We use to do this all of

the time when we did studies through the national institute of health. They realize that occasionally patients could not give informed consent and there were very loose guidelines as to when you can apply this exception to informed consent. If you got two physicians that were not involved with the research project to agree that this patient qualified and it was a safe enough intervention for the population at hand. It was very loosely done so the federal government, the FDA in particular, drafted guidelines that went through the house and senate and ultimately through the president's office that became effective November 1, 1996 and this is the exception to informed consent guidelines. What the specific criteria to apply those exceptions you must have an intervention or a drug that shows benefit over risk and that stands to reason. Someone is not going to be able to be giving consent chances are if they were to give consent or be able to give consent if the risks outweighed the benefits nobody would do that. The balance has to be towards benefit. Especially when you are trying to use the exception to informed consent. The

informed consent process must be impractical. Clearly when you have a life threatening condition the care of that patient is the utmost paramount importance and to sit down and try to give informed consent which if it is truly going to be informed consent requires a good 30-45 minutes of interaction with the patient and/or their families. So that clearly is impractical in this patient population. If you utilize the exception to consent, you will not adversely effect the patients right meaning that when they wake up they are able to decline further involvement. It is not going to put them in a position where they feel like they have been inappropriately used. Lastly, the criteria states that you must have full disclosure as soon as the situation is practical to inform patients that they have been involved in a study and full details of what that involvement is and what the risks and benefits of the protocol

is.

Q(Thom): Why is this particular study an exception to informed consent.

A(Thom): Well clearly our most severely injured patients are not going to have a situation where they can participate in true informed consent. Their life threatening situation makes this totally impractical. Because trauma is totally unpredictable often times our severely injured patients do not present to our emergency center with next of kin or legal guardian immediately available and if this study medication is going to be effective it needs to be initiated within 60 minutes of the patients arrival to the emergency center. So the practical natures of this state that often times our most severely injured patients do not have someone who can speak for them. In that case the next of kin cannot participate in the informed consent process either. If we did not have the exception to informed consent, we have a large population of patients that we would have to use standard therapy on and accept the fact 40% of those people would die consent will be obtained if it is feasible to do that before the study medication is infused, that definitely would be done.

To summarize, this research project has a very vulnerable patient population. Vulnerable in the sense that they have tremendous, they have a high incidence of having multiple medical problems if they survive and there survival is not certain by any means. Forty percent (40%) of them will die as a result of their injury. This medications seems in prior studies to be safe and beneficial. Because of those two things we believe and I personally believe that this medication has a very good chance of improving the survival of the patients that I take care of everyday. To make this process work especially when we use the exception to informed consent we really need to make our interaction between the hospital, the review boards of the hospital, the doctors that care for patients and most importantly

the community all on the same page. That we know what our problems are, we know what we are doing about it and we all have the opportunity to voice our concerns. That is really why we are here to do today. I have been long winded and I am going to sit down and give you the opportunity to share with us your feelings about this study, the concept of exception to the informed consent and any other issues you would like to bring about.

Q: What are the risks of the drug?

A: As I said, the most common risks are the discoloration. That is not a big deal. The major risk of this drug is high blood pressure but, again, that is the effect that we are shooting to get in this patient population. If I gave this drug to you it would increase your blood pressure.

Q: So my blood pressure would get so high that I would then have a stroke.

A: Not usually. It has happened in patients. In fact there was one patient where they used this drug in a patient who had a stroke and the blood pressure went up every time the patient got the drug and ultimately the individual died from the stroke and the benefit that was supposed to have been achieved that is you improve oxygen flow to the brain. While this individual died from this stroke and we could not say whether or not that was made worse by the high blood pressure. Clearly he had a stroke before and that is why he was getting the drug. In the population that we are going to be looking at they come in with a low blood pressure and the medication tends to make their blood pressure rise to normal levels sometimes not even to normal levels depending upon how severely the low blood pressure is. Even though that is an anticipated effect of the drug and occasionally we might see a transient high blood pressure it is not expected to be often.

Q: How many people were studied so far?

A: With this drug there has been 700 patients that have been enrolled in this study and as I said ...

Q: Have they been all trauma patients?

A: No they have not all been trauma patients. Two-hundred of them were trauma patients, another 200 were cardiac patients and there has been studies with renal failure and stroke patients. The effects in those populations are all taken together the adverse effects have been quite infrequent.

Q: Will you give more information on the shelf life? What happens to ??

A: The reason the Red Cross does not use blood that has been on the shelf for a longer period of time is that the blood levels even though the blood is cool and still metabolically active, meaning that it still uses up energy in those sorts of things it becomes to affect adversely the ability of the red cells to stay together so they break apart and that the Red Cross feels risks of that is too high. In the process of making this drug DCLHB the problem area is essentially stripped away. The coating of the red cell is totally removed so that you are left with the important part of the red cell that being the part that carries oxygen and that is maintained normal in this process. Stabilized and safe.

Q: Have they found any other successful uses for this blood that is lost?

A: People have been trying to make this type of medication for quite some time and the trick, again I am not an expert on the processing of the medication, the trick is to be able to make it such that it remains stable and the cross-linking process that Baxter has been able to create here makes the hemoglobin stable. If it is not stable, then it does not carry oxygen well. This is the first drug where that stability has been created. This whole idea of blood substitution has been going on for about 30 years.

Q: Other folks have gotten to this point and have done a trial and it has failed?

A: It has not gotten out of animal studies because the effects of the medication without this type of cross-linking has been adverse.

Q: This is the first one to step from animals to humans?

A: Correct.

Q: What other area of concern is has there been any demographical look at the target? Most trauma patients probably here in Philadelphia would be from a certain group such as young black males? Have they been tested subjects? Is there any safe guard to make sure that sex is not a concern? Race and economics?

A: Again, I think that a study protocol outlines who can be involved in the study. Male or non-pregnant females over the age of 18. They have to meet the entry criteria of being in shock or having an effect of low blood pressure and they have to have evidence that they are bleeding.

Q: What they have done to 700 people is that you look at that group and see if they have met those criteria.

A: We have not done that with 700 people. Seven-hundred people have been enrolled in human studies they have not all been trauma patients.

Q: In that group do you have the demographics?

A: I do not have the demographics.

Q: Can this be done double blind.

A: It is very hard to do this study double blinded and the reason being that the medication is red and it is hard to administer something that is colored and then truly be double blinded. As a scientist that is the way you want to do things. So that there is no bias to

anything. However, in this particular trial that is impractical and the reason it is impractical is that as an investigator we want our investigation to go on separate from the patient care activities. In other words the premise of this study is that the trauma patient regardless of who that individual is will get standard care and the only thing that is going to be different is that some of them are going to get the study medicine so that there is going to be a group of people that are going to be caring for the patient taking care of their injuries, doing every thing to get them ready for operation if that is necessary or to evaluate the full extent of their injuries. Those people are taking care of the patients and there is going to be another group of people that will take care of the study. Whether the patient gets the drug and if so that individual or individuals will administer the drug.

Q: In my view in Philadelphia. I can't expect black child to get the same treatment as equal or white are!

A: I do not understand why sir.

Q: Because they ??? I mean just the way the society functions in the real. The same treatment is not given to every patient and I can see a subjective group of people looking and deciding which one will be tried on by the fact of that the hospital will ?? and if you mess ??? child you would have a serious law suit. If you mess with this child that might be homeless or coming from broken homes they probably won't be ???? I am not accusing anyone..I lived in this country for years.

A: While I am not acknowledging that either but I hear you and I think that (Another person)I do not mean to cut you off...a good example of what he is talking about here. I think that he is right on. Let takes the hospital here for example okay. Tuskegee movie ???? and last night when I turned the TV I saw the story of this black male ??

Alabama and Mississippi. I saw that and both people even ?? More people have the tendency to be something because some can make decisions. ???? Lets look at the hospital here, I have been involved with the clinic here. I live in North Philadelphia. There is a great mistrust of this hospital. For years I have been up here with doctors involved with people here at this hospital because folks down there they are treated like dirt and everybody that comes in black they are treated like dirt. Getting back to what he says now with all going on and he is treated that way but it seems that in the hospital lacking trust there is going to have to be some good public relations and I am glad to see you making the first step by bringing community people here. I mean some good public relations .. I cannot speak for all of Philadelphia but most Philadelphians who bring this to the Allegheny West community of North Philadelphia some questions are going to be raised with the atmosphere of mistrust and that movie I saw last night about that the black men. I am glad to see that you are going in this direction but I think before you go into this black community there has to be a lot of public relations to be done because of lack of trust especially at this hospital. We are not just not?? For the years that I have been in N. Phila. 15 years now, I was up in Mt. Airy and my baby was born here. It seems to me that over the years it just seems that the equal calm to this particular hospital and the hospital has got to be body line who you are. Like I say everyone is treated like dirt. Alright. This has to be a trust system built up here to make this point. When poor people come you are talking about basically black males in trauma. We saw ??/ high blood pressure in N. Phila. It makes me question about that. The relationship of the hospital to the community and to come to us I am not saying that it is not good but I do raise questions about bringing it to us who will be effected.

A: The genesis of what we are doing today is just that because you know the community

better then I even though I have been serving this community for the last six years in the capacity that I have, I have a very jaded involvement. I see patients when they are severely ill. You have a better understanding of the community and that is exactly why we brought you here and I appreciate what every one is saying. Let me respond to the concerns that you have about the minority, underprivileged regardless of color, creed . You are right, in the past they make up the majority of the people that would fit into a study like this. I would say to you, however, the results that we have right now would suggest that if you leave status quo 40% of those people are going to be dead. That is not acceptable to me and I would think it would not be acceptable to the community at large. Now I think that we have to be fair and that we have to convey that fairness to the community so that they do not have the impression that they are guinea pigs or any other negative effect of being involved in this study, but if we can't do studies in this population because of our prejudices and our past experiences then we are not going to be able to move forward and make a positive effect on this population.

(Person) Not just minorities but many of the studies in the past have singled out males with the exclusion of females and they come up with results but they can't apply to everyone.

(Thom) I agree with you.

(Another person) ?????????????????????? I think you have to face reality. What you will be facing. Before this became Allegheny Hospital nobody from Women Medical came down to N. Phila to bring nothing to us. All of sudden now we found AUH has become a big business and down at the bottom of the hill in N. Phila we are cared for when the big business comes around. What about they cared less because we came up from N. Phila here before and we were treated like welfare people. When I brought my wife here to have my

baby born until I pulled out my card and I showed the resident reverend doctor. Are you a minister? Your wife in the school. You come over here while other black folks are still sitting there. All of sudden I am not talking about ?? okay all of sudden that this is big ??? Clinic in the community that is something we could have used 15 years ago. All of a sudden you want to use a drug okay to include the community. My question is not against what you are trying to do my question is that it seemed like nobody cared until this thing became big business. Now these kinds of questions are being raised at the bottom of the hill. You understand what I am saying. That is a very vital issue. While all of a sudden now here is a big thing to give to the community when before all of this happened we were nobody at the bottom of the hill.

A: I cannot answer that question and I think you are right. Maybe we should have been doing this 15 or 20 years ago.

Q: I am not against the drug. The question is raised that why

Sally Hilton: Maybe we did not have the resources.

I say we need it, but I still have to raise questions when you come down to the big business. I am not against the drug I say we need it okay but you say that you know nothing about the community that raises ??. Here is a doctor who knows nothing about us.

(Another person) He said in the capacity that you know. He said that he sees them when they are laying on the table half dead. But when I look up I still see a white doctor who knows less about me from my community. That should not be ??. I am not against the drug, I am not against the doctor but the flag goes up and say hey look that's what happened in Alabama. Suspicion. This is what I am talking about. Suspicion has to be eliminated in order for this to happen. I am not fighting. In order for this to happen it has

to be dealt with.

(Another person) I think that is why we are here.

Exactly, that is why you are here.

(THOM) In response to that you are absolutely right. Physicians should be providers of care which means reach out into the community, however, we also have a practical side. There is 24 hours a day, 7 days a week. I have participated in the role that I have in the community trying to promote bicycle helmet safety in our youngsters. I have been very vocal about domestic violence what we need to do about it before we can begin to bring this problem to the forefront so again ...

(Man) I am saying that when you come down you have to face reality. These things are going to pop up and I am just saying it is best

to deal with him get it out so this thing will happen. If you do not do it it will never happen.

(Sally Hilton) and that is why we need you here.

(Man) I have one comment and one question. I am Pastor DeHeymand and I serve a group in East Falls for 10 years. I live just down the street. I am not at the church in East Falls. What you said I find very interesting and I am going to take a risk and tell you why. Because the people in this community (the old timers) still refer to this place as Womens Med. But I have heard just the opposite of what you said from members of my congregation. They will say to me that I sat in the emergency room for 1 hour because I wasn't the right color (white). I always thought it was the reverse and now I here what you are telling me. I am just making a comment and I don't doubt for one moment what you

say I am just saying that I heard because I am white.

(Thom) What I hear from both of you is that we have some work to do in providing better service.

(Women) We are all suspicious.

(Pastor) My other question is that this will show my stupidity as a lay person If a trauma person comes in and they are a list of drugs in that person's system or whatever does that create an adverse effect on this procedure of this drug.

(Thom) Again that is a common phenomenon that trauma patients often times come in with various street drugs. The actual answer to that is that we do not know. It shouldn't in the sense that this medication will offset the effects of bleeding. The patients who receive this drug have to have evidence of bleeding and low blood pressure. So if there is some other medication that could be causing or contributing somewhat to the picture how it will interact with the medicine we do not know.

(Woman) I do not think that you are ever going to get rid of the suspicion that black people or people of different color have towards the hospitals or whatever but I think that it is imperative that people like you Reverend and everybody who has relations with their community to go out and tell them what is going on because I agree with what you are saying and everything and I agree to that you are never going to get rid of mistrust but if people can have your reassurance that this is okay and that you should not be afraid or that this is a safe thing it will definitely help.

(man) that goes without saying

(woman) I am just saying that if it is safe and you think that is safe could you support this research project.

(Man) What I was wondering because of the mistrust is that you should go to the black pastors and to individual churches. When I saw Rosewood I was reawakened. In society like this and the government supports that stuff. They were paying for it. When you come to a community I have the responsibility of my people to raise these kind of questions and to be certain about these kinds of questions and to know where the doctor is coming from and the hospital is coming from even with the change of big business. I am one of those who would say I think that it is needed. When you come in I want to know what is going on, how is it being applied and these are the kinds of questions to protect the community and the people that I serve. I think that you are right. I think that wrong step would be not to go to the community organization because they are political but to go to pastors and those churches and get the black clergy to endorse it. Do you understand what I am saying?

(Another) Being political.

(Rev) Not exactly being politically but in my community it is usually the church that takes the leadership. The people respect the church. There is a large number of people in church on Sunday morning. I think you should go to the black clergy to invite Rev. Patterson and talk with him. I think this would be a good thing but that is just my opinion.

(Thom) That is why you are here. I would like to make one comment to ??/ experience. The government was clearly wrong and I think that anybody who is alive now realizes how wrong that is and I think that change in the federal government and how they view ethics in general is in large part because of people like yourself that have been there to say now wait a minute. Wh[illegible]

being taken into consideration. I think that the federal government could never repeat an experience like that just because of the community activitists like yourselves.

(Man) The system selection is ??. That is not in the hands of some human that will say we will give him some, no not that one. We have to trust this person. Is there any scientific way? Everyone gets a number and it will be all number threes today etc.

(Thom) The problem with the whole process of enrollment is that fortunately these patients don't come in every day because if they did we would have a lot more dead people that ??. So the best I think that we can do is to have pre-established guidelines. This is what you have to have to be considered for enrollment and if you have these things you do not fit and it does not matter if you are President Reagan's daughter or if you are my daughter. If may not allay some of your fears but if my daughter should ever be in a situation like this I would like to see her get this drug. That is probably not going to allay your fears about looking and seeing well may be this person should have it and this person shouldn't. It all depends on whether you think this is a beneficial treatment and I my bias if you will in reports that I have seen is that this is a beneficial treatment and if I could give it to everybody I would like to, but scientifically I cannot do that because I have to see proof that in human in this population it is effective. We have been tested by ?? for four years the fact that you have something which may save a life. When you come to a hospital you want the person to get better and the life to be saved. Red, yellow, green or blue you want that person to get better. I think that the drug itself is something that should be used and used throughout the city in all hospitals.

Q: How come this hospital was chosen and not other hospitals.

A: The hospital has been chosen because of our reputation as a trauma center. There are other trauma centers in the city that have also been invited to participate in the study. For example, Univ. of PA, Temple, Einstein and my colleagues at those hospitals have just not for whatever reason been as efficient at getting this study to this point. But yes it is not like we are the hospital. I feel privileged to be involved in this study.

Q: As far as the issue ?? (PGH) general hospital ?? chose that hospital for studies because in medicine if you chose a hospital we think but now we are not sure because it had the worse cases there. It had the poorest people and the sickest people. So that would be the hospital that was chosen to do the study because you had the worst of everything there.
A:(THOM) You may be right, I do not know. It was long gone before I came to Philadelphia. Those large city hospitals also had the best doctors. The people that were moving the cutting edge of science that is why the study was brought there. I am being political here too.

(Man) But one of the things that happens is that the population that is tested would benefit from the good things that come out of the test some of the paranoia would subside. The problem is that the test and 4 or 5 people might die but something good comes out of it then that population does benefit. Is there a guarantee.
(Thom): There is never a guarantee.
(Man): Who owns Baxter?
(Thom): I have no idea who owns Baxter. That is a good question. (Man): Is there a way to get that information.

(Thom): We could certainly try.

(Woman): We have no reason to believe that Baxter is not on the same page as we are. We have participated with them on several studies not just this. We have had a lot of success and this hasn't been an issue but we can certainly look into that.

(Man): It would interesting to see who owns it. This hospital has changed quite a bit. AUH/MCP not East Falls.

(Woman): I have to be involved in changing this sign on the front door so you can imagine

(Man): So this hospital has changed ownership.

(Woman): Actually we have not changed ownership in 10 years. We have been with Allegheny for 10 years.

(Thom): We just changed the name.

(Woman): The other part of suspicion ???. I use to work for a doctor and we did a study with a diabetic drug and treated an old diabetic patients and I wonder if he did that study because he owns stock in the company. There is that kind of suspicion.

(Thom): That is not the case. That is too easy. Christine you have been kind of quite. What are your thoughts on this?

(Chris): I'm listening. The trauma patient that comes in will be mainly the trauma population.

(Thom): It could be gunshot wounds, flank pains, falls, etc.

(woman): With the consent policy. This will be randomly done. ????

Cannot hear her. Will it be noted on their medical records that they were taking the drug.

(Thom): Yes

(Woman): ??? family members or themselves.

(Thom): Unless the family is present. If they are present, then we will check to see if family is present and if so we will conform to standard informed consent. As I said often times the situation does not allow for that ideally you might have the patient do that consent, however, if they have a blood pressure of 60 that event right there is coerced. You can tell that patient anything and they are going to say of course fix me I am sick.

(Woman): I am going to give you a scenario of Friday night, 1:00 am you get a gunshot victim who was shot six times in a particular area . It is definitely trauma.By the time he gets here it has been awhile. How would he be prepared? What would the determination be when they come in?

(Thom): It is really the severity of their shock. If a patient comes in and is in shock and there is evidence that the bleeding caused that shock because you could have a severed spinal cord and have shock but it is not from bleeding. This medication will fix that problem. The vast majority of people that are injured that come in in shock are in shock because they are bleeding. So if they are over the age of 18 and they are a non-pregnant female we would find out simply by doing a urine test to check and see if they are pregnant and there evidence of bleeding then that person is a potential for the study. Now that doesn't mean that that individual will get the drug. They will say this patient meets the entry criteria. You got to an area that has a bunch of envelopes and the first envelope on the top is chosen and you open it and the envelope says study drug or it says placebo. It is not blind that in the sense that we know what the patients will get but we do not know what the patient is going to get before we enroll them. In other words, if the two of you came in I cannot sit here and say I am going to give Mr. ?? the study drug and I am going to give Mr. Simmons the salt water. I cannot do that. But if we both meet the study criteria

I reach for one envelope and I reach for another envelope. You might both get the study drug or you might both get salt water. The envelopes are identical.

(Woman): It is blinding.

(Thom): That process is called randomization. Blinding really refers to something else but in the sense it is blinding.

(Woman): Back to discrimination. Is there a possibility that women would be discriminated against here because if you are coming in and you have to check to see if you are pregnant and if you can't check within the hour they cannot get the drug.

(Thom): The test that is done to determine pregnancy literally takes 30 seconds. You take a drop of urine, you put it on a glass slide

(Woman): ??? bladder or something?

(Thom): All of the patients in this process are getting their standard care and have a tube placed into the bladder. It is one of the thing ?? ??

So that process even though it takes another step is done expeditiously. I do not believe that women would be bias in this study.

(Man): What is the time frame for the study to begin?

(Thom): The process that we are going through I would like to euphemistically say is our community consultation. In the sense that what I had asked Sally she was very good to bring you together as key members of the community to just hear what the study is about and what we had done we had put together some drafts how we could communicate this study and our intentions to do this study to the community and what our initial thoughts were is that we would advertise in local newspaper and we would send out specific letters of invitation to key individuals which we hope you will help us identify to inform of our

intention to have community meetings and the other thing that we would like you to help us with is to try and identify key areas in the community where we can have these meetings where we can get the most amount of awareness.

(Ruthann): Maybe it would be a good time to talk about some of those different communication kinds of things. My name is Ruthann Daily and I am from the hospitals Communication Department. Essentially we want to be able to get your feedback on the kinds of ways we should communicate to the members of your communities. What are the kinds of things that we should do to let your community members know about this study and we are not doing this study right now and that is something that I just wanted to make sure that we are all on the same page about. We are not doing it and we want to get the reaction before we decide at what point we are going to move forward. So I think that some of you may have this. This is just a list of the communication activities that we want to do. Okay. The very first thing that we want to do and I think what is essential is for us to host community meetings. We want to go out into your community and I think your suggestion of connecting with the churches is a great one. We will see you next week. We would like to get your feedback on where we should go, the best places to be and whether or not we should also invite people here or whether or not it is better to go out into your own environment and meet with you and the community.

?????

(Man): I think it would be better to come to the community. Then again I express the church gatherings and not during the week, but I would like to have a meeting like this right after my church on Sunday morning when everybody is there. It is hard to get people to come during the week. Now what I did before in a meeting. I had about 250 people in

church and I said that the pastor wants you all to say about 15-20 minutes. We will do the benediction after. I invite the folks in, we had a very good meeting and everybody was concerned and got involved. Meetings during the week is rough but I think that even if you talked to pastors?? during that service and we would like for all of you to stay at the service. If you can get into deliverance and on fire I do know churches like my church, ?? church's, etc . The idea is Sunday morning I would introduce you to the congregation but at the church. I think that that is the best idea.

(Ruthann): That is a great idea.

(Man): I think that we need more written material.

(Ruthann): I would like to share some stuff with you.

(Man): Intellectual and scientific minds that are respected and we have Rev. ?? here as one of our most respected intellectuals. We want folks that we respect to screen this material and if they say ???.

(Ruthann): If you have some folks that I can work with directly I think that would be great. If you have any suggestions for me. In addition to hosting community meetings, we want to be able to advertise those community meetings in your local newspaper so that everyone is aware of when they are going on.

(Man): Flyers and so forth especially elementary schools because parents are more involved there and they come in and children tend flyers home with them.

(Ruthann): I would like to pass out a draft of an advertisement. This is an ad that we would like to place in some of the local papers and there is a list here that I have made with after my church on Sunday morning when everybody is there. It is hard to get people to come during the week. Now what I did before in a meeting. I had about 250 people in

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(Woman): I think it is important to go to high schools especially the urban ones around here. ??????? You should have a doctor of the same color of the school so that people can ???

(Ruthann): That is a good idea we can definitely pursue that. I know that it is difficult to just give your immediate reaction to the ad and when we connect at a later date we can get some more feedback but this is the kind of approach that we think we are taking at this point. Something to grab peoples attention. We are not going to be able to give them all of the information in one advertisement in the newspaper but we want to be able to say this is what we are interested in doing, come in for more information. These are when these meetings are.

(Man): With Allegheny West we have a community fair that was set up 3 or 4 years ago. Alleg West does a terrific work. I think a booth would be a good idea. I think that when a crowd is there around the stand and the dancing is going on it would be a good time for the hospital to walk up and hold the crowd from the community and do a slight presentation about this.

(Ruthann): When is that event?

(Man): It is in June no date yet. I think to do that you need a large amount of people at one time and then they can go to the booth for more information if the hospital would have a booth.

(Thom): One of the things that I would like to focus on is that people are dying all the time and the sooner we can get this trial going the sooner we may be able to benefit some of those individuals. Again, I think that your input is tremendously valuable and what we

really need to do is to come up with a practical way of doing these things in a timely way. There has to be some way of doing it in a period of time that is reasonable and the number of events likewise has to be fairly reasonable because again I have patients that are our community that I take care of and I have to continue to do that ???

Cannot hear

(Man): How many people do you have?

(Thom): It depends on how much conversation is ??.

(Man): There is going to be a lot of conversation. ??????????

Movie and that is the category you might run into ????

(Ruthann): Present the whole scanner up front. You say this is what it is going to be.

(Man): Put the actual scientific data and the research that is being done. This is it and be as technical as you can in a newspaper. Folks can read it.

(another man): One thing that he mentioned that I think is very important that we found this out is that the doctor here let us see some black faces make some presentations about this. In churches you should uses doctors of color when we are having a meeting.

(Ruthann): Forgive me I do not know your name but you mentioned about putting out information. Is this the kind of information?

(Man): No I am talking about the actual technical information. What is the drug? What does the drug do? Have a picture of the cell you know how they do . You see where oxygen is going the cell is like this, etc. People understand that give it to them and then once they read it some will not understand but there are folks in the community will understand it and they will say this makes sense. The facts are good.

(Ruthann): Actually I was not capable of understanding it. I do not have that kind of

background. We did this altogether and kind of worked it out so that it was easy to understand.

(Man): all of this sounds good but the kind of folk at my church some of them okay you have to break it down.

(another man) there is some trauma nurses in the congregation who will understand this and your congregation will listen to them but they need to know.

(Ruthann): We would definitely want to have Dr. Santora on different radio shows. We sponsor one on WWDB that we have plans for Dr. Santora to be on at the end of the month. Somebody said WDAS and we will definitely look into WHAT that will be really valuable.

(Man): I think it would be good if you have a meeting with these organizations. One is called BUMP Black United Methodist Preachers. That is just a suggestion because you are talking about ?? black clergy who are methodist in Philadelphia. The next thing is to get in touch with Ralph ?? and then let him take you to the Black ??.

(Thom): Obviously by your own suggestion you see the altitude project and the enormity of this project as we try to reach the community. Because what really constitutes the community. We know that we service the immediate area however our helicopters go 50 miles and any body from any where could be driving Route 1 and have a car wreck. So that issue of community. What is the community is really an important one for large cities like Philadelphia. I think that we have to make the effort to try and be as broad in scope with our effort as possible and the suggestions that you brought to the table are very good some of which we had thought about others we had not. The input that you brought to me is particularly important and I appreciate that.

(??) You have Constance Clayton in a part of this hospital. You are already in contact with ???? which is a huge piece of this community. There are organizations that you are working with now. Go internal and go through those organizations. You already have the relationships.

(Woman): Are you a physician in research?

(Man): I work with young minds. I am the principle of Germantown High School.

(Woman): I do not mean to put you on the spot but what do you think of this drug and this proposal. You suggested that he is somebody that he was somebody highly respected.

(Man): He is someone I respect.

(Principle): I apologize for being late as it works in the schools there are emergencies and I had a couple to handle. From what I heard I think that it is a fantastic idea, I think that it is a fantastic opportunity for this community to be on the cutting edge of something of this scope. I think that those of us sitting here and those associated with the hospital ought to be about the task of disseminating information and disseminating it in a manner that people buy into what is happening, recognizing that this is an excellent opportunity and not ??guinea pigs but the fact is that it is life saving and that it is something that is going to be widely disseminated in a short period of time. I think that we are doing the right things in terms of strategy.

(Woman): You have no suspicion at all?

(Principle): Not at all.

(Man): I do have a suspicion but I think we need to talk about that and work that out. Reality is reality. I have a suspicion because of who I am. I think we need to work those things out as soon as we can but I am for the program.

(Ruthann): Do you have anything to add Dr. Santora?

(Thom): Well again that I appreciate your time and input and the only last thing that I would like to ask is part of the process of doing this exception to consent is after we do the study and say the community supports our efforts and we as a community believe that this is going to be beneficial and we go forward and do this study we are mandated by the new federal regulations to bring this information back to the community as a whole so not only are we asking for input on how to get this information out to there but also once we have what we set out to show good or bad it is going to go out to the community. Would you be interested in being whatever that may be we are hopeful that this study can be completed within 18 months. The idea is to enroll 850 patients nationwide in 18 months.

(Woman): When are you starting?

(Thom): Again, it depends on what it takes to increase awareness to our community and what we feel is the degree of the project that we have in front of us. We need the community because the feedback that I get from these meetings, from the community meetings, from the talk shows all of that information has to go through our hospital board that reviews research projects and they are going to hear all of the comments that have been made today and they are going to have to decide as a representative of not only the hospital but also the community at large does this serve our interest.

(Man): What is next?

(Thom): I think what we need to do is to take the information that has been brought on the table today and put together a package for disseminating that to our communities and how you want to be involved, if you want to be involved further in that process I would certainly welcome your involvement each and every one of you and the process will have

to be fed back once we actually go into the community to the hospital board and if they are comfortable that the community as a whole feels that this is something that would be beneficial then we will begin enrolling patients but not until that time.

(Woman): What if it is not well received within the community?

(Thom): It will not happen.

(Principle): What then are our benchmarks in other words how do we know when it is a go or no go. What are our standards of assessment?

(Thom): That is a good question. We could talk about that. If you would like what we could do or what I could do is I can bring before I get the results generally available from the hospital board I can bring this group back together and share those results with you. I would be willing to do that. I feel like I owe you at least that much since you put two hours of your valuable time today. That is up for discussion. Those of you who would like to do that I can contact you if not that is okay.

Can't hear.

(Thom) Is anyone else is interested?

(Woman): Lets do it like school. How many would like the reports and be a part of the study. Raise hand. Everyone. Thank you.

(Thom): Thank you very much.

Attachment 14

Community Consultation Meeting
March 24, 1997

Present: Mr. LeRoi Simmons
Mr. William Sconniers
Reverend Thomas Sligh
Officer Velma Dean
Ms. Serita Reels
Vincent Cowell, M.D.

1. Dr. Vincent Cowell was introduced to all community members present as a co-investigator on this program.

2. The need for additional support as back-bone individuals or groups prior to general public disclosure was discussed in detail. Reverend Sligh felt strongly that additional support amongst the clergy was needed. He recommended strongly that we obtain the confidence of Reverend Blanks.

   Action: Reverend Sligh working with Sally Hilton will set up a meeting with Reverend Blanks.

3. Additional contact personnel were felt to be needed in each of the key areas that constitute our immediate community. Those areas include: East Falls, Roxborough, Germantown, Mt. Airy, North Philadelphia, and Allegheny West.

   Action: Each representative from their respective area will generate a list of influential people along with their addresses so that a specific letter of invitation to the town meetings can be sent. Sally Hilton will be responsible for collecting these lists and transmitting them to communications.

Respectfully submitted,

Thomas A. Santora, M.D.
Associate Professor, Department of Surgery
Principle Investigator

TAS/lh

This is Medical Frontiers. The show with current information on medical breakthroughs and answers for your health care questions. Medical Frontiers is hosted by Dr. Joel Posner and is brought to you by Allegheny University Hospitals, and by St. Christopher's Hospital for Children. Dr. Posner urges you to take your health seriously and to rely on your doctor for definitive medical advice about your individual health needs.

Exploring Medical Frontiers with Dr. Joel Posner. Only on "the" talk station, 96.5 FM, WWDB.

(JP) Imagine this, you're riding in the street and walking in the street and someone shoots at you with a gun. You're brought into an emergency room, you're bleeding, you're blood pressure is low. With the best care, you have about a 50% chance of survival.....with the best care. Why do we have such an abysmal record in trauma care? It's because it is extremely difficult to do research on those kinds of things that may save the life of a trauma victim. You're brought into the emergency room, generally unconscious, often alone. You can't give consent for studies and so research into trauma and its treatment has really lagged behind a lot of other research. My guests tonight, Dr. Tom Santora, Associate Professor of Surgery, Associate Director of the Regional Trauma Center, Pam Crilley, Assistant Professor of Medicine. She happens to be the Director of the Bone Marrow Transplant Program, but more than that, she is the head of the Research Review Board for Allegheny University. They have identified, or nationally has been identified, a product that may help to save the life of trauma victims. The problem, how do you study it? Right now, Allegheny University, particularly MCP Division, has gotten permission to study what may be a life-saving new drug for trauma victims. The University has decided in its wisdom that they will permit the study if, and only if, the community wants it done. I've asked Dr. Santora and Dr. Crilley to come tonight to explain this study. We're supposed to be talking about dizziness, but I think this is so vital that I asked them to come tonight to explain the study and to as you who are listening to us to call and give your opinion about whether such a study should be done.

Dr. Santora, it's true isn't it that the leading cause of death in people 44 and under is trauma?

(TS) It is. Trauma is a disease that can attack anybody; race, creed or color, but in fact, it tends to be the leading cause of death for the most vital of our patients, those under the age of 44.

(JP) I wasn't exaggerating when I said if you're brought to an emergency room, even one as good as

the one on television, If you're brought to an emergency room with a low blood pressure from bleeding, you have a little better than a 50% chance of surviving.

(TS) Unfortunately Joel, you're right. The problem is just as you have described. We have been handcuffed with our ability to introduce new therapies into this situation because oftentimes these patients are so ill that they can't give informed consent, which is a paramount process for research subjects.

(JP) And the fact of the matter is, if you present to a doctor with heart disease, if you present to a doctor with bowel disease, if you present to a doctor with cancer, that doctor, he or she, can explain to you a study and you can yes, I'll be part of that study, so then we can develop things. But, think about it now.....you're brought into an emergency room, you're unconscious, you're bleeding, usually you're not brought in with your family, so who gives consent for a study, so the study isn't done. Dr. Crilley, you protect patients by making sure that none of us, I have to tell you, truth in lending everybody, I personally am heavily funded by the National Institutes of Health, particularly the National Heart, Lung and Blood Institute. A lot of my staff and I live off of doing research studies. We publish and so for us it is very important to do research. But, Pam, before you'll let me do a study you want to be sure that all of my subjects are properly protected. Can you explain how that Board works?

(PC) Well, basically, it's a Board that is made up of scientists, physicians and lay members from the community who get together and prospectively review potential research projects involving human subjects, and what we're really looking for is that the risks of the study and the benefits of the study are clear and explained to the patient and that the study is extremely well watched for the duration of the study. So that if new information becomes available as the study progresses, that the IRB would be informed of that. And, we want maximal protection for the subject and also want to know that the subject is well informed going into the study.

(JP) For example, in the study that I have just been funded for to look at alternate treatments and lifestyle treatments for high blood pressure, I had to go through your board to make sure it was safe before I could even ask for money. You insisted, your board insisted, that we have an internal review committee that is not attached to the study to make sure I was protecting my subjects and the National Institutes of Health

wants an external review committee. So, everybody's watching me like a hawk and that makes me feel comfortable. But, how about in a case like Dr. Santora, where he wants to study a new product, an experimental product, its been tested in animals, shown to be effective, tested in volunteer human beings, shown to be safe, now you got to test it in trauma victims. How do you protect those victims?

(PC) Well, I think that a lot of thought has gone into the concept of looking at patients who can't give informed consent easily or their legally authorized representative, and different disciplines such as neurosurgery, cardiac, in addition to trauma, have gone to the Federal government and asked for some guidance in this and to set up certain conditions under which consent could be waived. And, this is a lot more complex, the whole process of obtaining consent is much more complex and there is lots of layers of people looking at this. A study such as this could not go forward if the FDA does not approve the study in addition to the IRB and it has to be closely monitored.

(JP) Now, the FDA has approved this study and you're IRB will only approve it if the community wants it done.

(PC) Yes, we think it is extremely important, as does the FDA, that the community in which you consider doing the research understands the purpose of the research and understands that the basic idea of it is to eventually improve conditions for these subjects who have traditionally been under-studied and denied clinical research trials.

(JP) So, they're denied clinical care and I'm going to tell everybody now that we're going to ask you to make calls tomorrow and tell us what you think about this whole business. Everybody in this community has got to tell us if they want this kind of study done and I'm going to ask Dr. Santora a few more questions in a minute, but let me remind you that if you have any questions you want to ask tonight, or if you want to tell us anything tonight about experiences you've had with emergency rooms or with studies and research, the numbers to call in Philadelphia and New Jersey, 365-4100, Pennsylvania suburbs 664,4100, Delaware 234-4100. Free call on the Comcast Metrophone and Bell Atlantic Nynex cellular systems. We pay for the call if you call us on one of those two systems. Tell us about the study Dr. Santora.

(TS) The research material is a blood substitute and we have been asked to participate in this trial of

extremely injured shocked trauma patients to try and see if this material, as you described has been shown to potentially be beneficial in animals and has been shown to be safe in man, but under these conditions of severe shock will it be effective in man is the real question.

(TS) How do you plan to do the study? What will happen? I'll be brought in for perhaps with my chest crushed, bleeding, low blood pressure.....what will happen to me if I'm in this study?

(TS) If you meet pre-established entry criteria, then you will be randomized or you'll be eligible for entry into the study and the randomization process is simply going to a drawer, picking out an envelope and deciding once that envelope is opened whether or not you'll get standard therapy plus saline solution or standard therapy, which includes blood transfusion, operation and large amounts of salt water solutions to support your blood pressure, in addition to this blood substitute. This blood substitute must be given within the first hour after arrival at the hospital if it's going to be effective. Many of the audience, I am sure, have heard about the concept of "the Golden Hour" of trauma. And, the idea there is to try and normalize the blood pressure and the blood flow to various organs to try and minimize the damage due to extensive bleeding.

(JP) And, what you're trying to do then is give people, during the Golden Hour, what may be a golden medication that may do something to help these terrible statistics, 40% of people dying of trauma, coming in with trauma and shock are dying. What do you say to folks who are listening to us who say it sounds like they're experimenting with human lives?

(TS) Well, we are experimenting with human lives. The situation right now is unacceptable for all of us who practice in this area. Meaning, 4 out of 6 people that present after severe injury with hemorrhage that creates low blood pressure, despite our best efforts in 1997 those patients die. And oftentimes, they are our most young and vibrant individuals, and it's a shame to see these people continue to die despite our best efforts when we know that there are potentially beneficial drugs and interventions that we have recently been unable to test in this population.

(JP) Just to let people know where you're coming from, you're looking pretty tired because you were up most of last night with two patients, one of whom you were able to save, another one of whom died

because of stab wounds despite your best efforts, and you were up all night with them.

(TS) That is true.

(JP) So, you're not just a person who is speaking from third and fourth-hand knowledge. What I would like everybody to do is this, call us at 1-800-PRO-HEALTH during business hours and say you are interested in expressing an opinion about the blood substitute study. You get to vote. You get to call us and tell us whether or not you believe this study ought to be done in the community. That number, 1-800-PRO-HEALTH incidentally is also the number you can call if you still haven't gotten your Health Tips. They were sent out about two weeks ago. If you want our list, our best list, of things you need to do for your health, call us at 1-800-PRO-HEALTH and ask for the Health Tips. We'll mail it to you free and also ask to express an opinion about a study that may show the way to save the lives of trauma victims. We'll be back in a minute. (Commercials)

(JP) Hi, you're back on Medical Frontiers. We're talking with Tom Santora and Pam Crilley. They're both physicians and both very interested in research. Dr. Santora is one of the noted trauma surgeons in the United States. Dr. Crilley is a hematologist/oncologist, but she is here in her capacity as Director, or President or Chairperson, what are you exactly?

(PC) Chairperson.

(JP) Chairperson of the Review Board that protects subjects in studies. Pam, why do we even need to worry about protecting experimental studies. Doctors wouldn't hurt folks, would they?

(PC) Well, you would think they would not and I think often they intend not to, but really the origin of the committees for protection of human subjects in the United States are based on atrocities in Nazi Germany, some studies that went awry in the United States with the Tuskegee syphilis experiment in Georgia.....

(JP) Just to remind folks, the Tuskegee syphilis study, patients were allowed to die of syphilis at a time when there was treatment just to see what would happen. We were all horrified when we read about that happening in the United States in the 40's and 50's.

(PC) That's right, and there is still repercussions of the Tuskegee experiment and as a result of that the Federal government has asked different boards to look at the protection of human subjects and to try to

obtain their informed consent and to make sure they understand the research before they enter into it.

(JP) So, how do you...now, if Dr. Santora deals with folks who come in unconscious, alone, dying, unable to give consent. How do you get around the need for consent? How do you protect folks and yet study conditions like this with studies that can be life saving?

(PC) I think that's a very difficult question and I think that the answer is that these patients have been under-studied, are in a life-threatening situation where there is insufficient scientific evidence to prove the best way to improve their outcome and that such patients need to be studied with additional safeguards and additional protection to try to make sure that their entrants are protected and we do look at potentially talking to family members, legally authorized representatives and hopefully the patient him or herself once they recover, if they recover from such a situation, and these types of studies will be reviewed with great scrutiny.

(JP) And what are the exceptions that are made Dr. Santora? I mean, how do you get around this informed consent? What conditions have to be met?

(TS) Well, the FDA has come out with a recent change in guidelines that was published and went into effect November 1, 1996, and it allows an exception to informed consent under very strict guidelines. Those guidelines involve situations where there is life-threatened processes. That, the research could not be done without the exception to consent. The benefit/risk analysis of the study or the drug is in favor of a benefit aspect of things and that if, in fact, there is family or proxy decision maker that can give consent, that consent will be obtained.

(JP) So, let me go back over this; the four conditions that have to be met are 1) the condition has to be life-threatening, 2) you have to have good reason to believe that the treatment may hold the promise of saving lives, 3) the person has to be absolutely unable to give consent and, 4) you have to agree that if any family is present you will check with them before you go ahead, and if those four conditions are met, my life is in danger, there's reason to believe you can help me with the treatment, I am out of it and unable to give consent, and my family is not around, if the community permits we will go ahead with the study if those four conditions are met. I wonder if people listening to me would like now to express an opinion as to

whether studies like that ought to be done. You can do that by calling during business hours 1-800-PRO-HEALTH and saying what you think about it, saying you'd like to express an opinion, but you can call us right here, Philadelphia and New Jersey 365-4100, Pennsylvania suburbs 664-4100, Delaware 234-4100. It's a free call on the Comcast Metrophone and Bell Atlantic Nynex cellular systems. Tom, you wanted to say something?

(TS) Joel, the FDA painstakingly came up with these guidelines, working some 2, 2 ½ years with very learned people, the lay people, ethicists and scientists in the emergency medicine area and these guidelines were drafted to make, what they felt, was the safest protection for these subjects and still allow the necessary research to move outcomes in the right direction. Now, there are other things that need to be done to undertake an exception to informed consent. Additional precautions to protect the rights of the subject. Maybe Dr. Crilley can add some of those, but the issue is if you can't get consent from the patients that you're studying, then the idea is to try and inform the community from which your patients are most likely to be drawn, so that before you undertake a project like this where you use an exception to informed consent, you go out into the community and you outline the study. You outline the problem and you inquire about their feelings, and those things are going to be very germaine for us as we move forward in this project because our community is who we serve and we need to have them understand that we believe this is a potentially beneficial therapy, but they have to believe it just as much as we do.

(JP) We're talking to Trauma Surgeon, Dr. Thomas Santora. He's Associate Professor of Surgery, Associate Director of the Regional Resource Trauma Center at Allegheny University Hospital. Dr. Pamela Crilley, Assistant Professor of Medicine, Director of the Bone Marrow Transplant Program. She is also the Chairperson of the Internal Review Board that allows all of us to do research or not to do research. She is in the business of protecting subjects. We are talking about the study of a potentially lifesaving drug on trauma patients brought in unconscious and alone. Do you believe such studies should be allowed to be done, particularly because they may save the lives.....how many folks do you think die of trauma every year in the United States?

(TS) It is a fairly consistent number and it's large. It's a 140,000 Americans each year die from trauma.

Most of those people, in fact, die as a result of major bleeding.

(JP) And so even if you could save less than one-half of them, you're talking about saving 10,000 people a year.

(TS) Well, more than that. Our study is not looking for the results that you saw in the 40's from penicillin where you had absolute cure. What we're really looking to do is to reduce the mortality by 24%.

(JP) I actually misspoke myself, I should have said 1,000 people a week, 1,000 lives a week could be saved if this and other studies like it showed the way.

(TS) Well, that may happen, but if we could see a 25% reduction in the mortality we would save, on average, about 35,000 patients a year in the United States alone.

(JP) So, 35,000 patients a year, you're talking about 2,500 people a month. Two thousand five hundred folks a month if this study and others like it helped out. And you will not permit the study to go forward without community permission?

(PC) One of the considerations the IRB has is to serial look at the study before it fully approves it. First, it looks at the scientific merit in the study and makes sure that the pre-clinical animal studies support the potential use in human subjects. The FDA also must look at the study before it's allowed to go forward and the IRB will decide after the community has given some input; community leaders and members of the community, so the IRB can help determine if they consider it a study that should go forward.

(JP) What do you think kills most people who come in in Trauma? What specific thing happens....are they shot?, hit in an auto accident? I mean, the folks you see at MCP, for example.

(TS) The major problem is that they bleed and when they bleed they reduce their nutrient flow to various vital organs, and the most important nutrient is oxygen, and that's where this blood substitute really has its most potential benefit because it actually carries oxygen as well as the hemoglobin in our own red blood cells. In fact, this material is made from human red cells that are no longer usable because they've been on the storage shelves longer than the advisable 42 days. The sponsor, Baxter Healthcare, has taken this expired blood, which has already gone through screening processes, they've stripped the coating from the red blood cells and they have done a chemical reaction where the material, the hemoglobin, is made stable

and still has the capability of carrying oxygen. Therefore, when you give this blood product, or substitute, to trauma patients they can carry oxygen to their vital organs and,

(JP) Let me just as you that, what I was asking was a different question. What is doing this? What is causing 140,000 deaths? Is it car accidents? Is it drunk drivers? Is it people getting shot, stabbed? What's doing it?

(TS) It's that whole spectrum and it is different for different trauma centers. In our particular trauma center, we have about 75% of our victims that walk through the door or roll through the door are victims of what we call "blunt trauma". However, the .....

(JP) Give me an example of blunt trauma?

(TS) Blunt trauma; a fall from a great height or somebody who has been involved in a motor vehicle accident. Those are our two leading causes of blunt mechanisms. However, the other 25% are from gunshot wounds, victims of intentional violence, where their mortality is quite high.

(JP) And, one of the patients you lost last night was stabbed multiple times by a lady who decided she didn't want to see him anymore.

(TS) That's correct.

(JP) Yeah, I mean this must be a tragic thing. How real do you think the show "ER" is in reflecting what actually goes on in your life?

(TS) Well, I mean, you don't fool around with any of the nurses like they do on "ER", but ...

(JP) Cause your wife wouldn't let you, but how real is what goes on professionally?

(TS) To tell you the truth Joel, I don't watch that program so I really can't comment on that, but I suspect that the ratings wouldn't hold up if it was anything near reality. But, certainly big city ER's are busy and I think that that's they depict. Some of the undertakings, I understand, are a little dramatic, but nonetheless, the emergency room is a hectic place and it's a spot where a number of our young people die and if we could do some of the things that are on the horizon and with this new FDA guideline for exception to informed consent, if we can get our community to see that this is a big problem for our young people and for people of all age, color or creed.

(JP) You think it can make a difference?

(TS) It can a difference.

(JP) I think Pat in Northwest Philly may disagree with you. Pat, you're on WWDB.

(Caller) Hi, I just wanted to ask, I didn't hear the very beginning of this show. What is the name of the product?

(JP) What's the name of the product?

(TS) The product is called, RECORDING STOPS AT THIS POINT AND PICKS UP BELOW.....

(Caller) If you're familiar with that, do you know why that isn't used more often?

(TS) Yes, Fluosol is a fluorocarbon. It also carries oxygen, but unfortunately, doesn't have the same properties as does hemoglobin and it's beneficial effects have not been as great as the preclinical studies have suggested with this product.

(Caller) Uh huh. Lives have been saved with that though, haven't they?

(TS) I'm sorry, I didn't hear that question.

(Caller) People's lives have been saved by use of Fluosol, haven't they?

(TS) Under certain circumstances I believe that to be correct. I'm not at all familiar with the full literature on Fluosol.

(JP) Pat, what do you think in general about the idea of doing studies on people who come in in severe trauma like this, hoping to develop techniques to save lives?

(Caller) The only thing that I have against that at all is that some people want absolutely no blood products whatsoever. So, that's the only thing I would have against that and some people feel that for religious reasons and then other people feel that for other reasons.

(JP) You know, Pat, I agree with you, but let me tell you what happens right now, if somebody, even a Jehovah's Witness who has very strong feelings against trauma, against blood transfusions, is brought into an emergency room and nobody knows that that person is a Jehovah's Witness, and if that person appears to be slipping away and needs a blood transfusion, he or she will get a blood transfusion. Now, if you know that it's a Jehovah's Witness you won't, but if you don't you will. And, one of the exceptions in your study,

Dr. Santora, is you won't take Jehovah's Witnesses in the study.

(TS) That's true. If we know that the person has a strong contention that they would not want to have blood products under any circumstances, then they are not a qualified candidate for the study.

(Caller) Right.

(JP) And, they'd be out of the study.

(Caller) Right. Well, I often feel that hospitals should at least have Fluosol on hand for people who wouldn't want blood.

(JP) Yeah, that's fine, but how about the use of some newer products that might be better. I mean the real question that everybody's grappling with is, how do you do studies on people who can't give consent and Dr. Santora is coming to the community and saying, I'm asking the community give me consent, you know, do these studies.

(Caller) Right. Well, the only thing I can thing of which would sort of be monumental was to have people signed for. For instance, if they have to go the hospital for something, while they're there, you know how you make a Living Will, or just give their.....

(JP) So, you think people should sign forms in advance...

(Caller) Yes.

(JP) when they're not hurt?

(Caller) Yes, at least they have the opportunity to do.

(JP) That's an interesting thought. Maybe with the driver's license or something. What do you think about that?

(TS) That's certainly a viable option. Unfortunately, that fits for all medical illnesses and, unfortunately, though most people say they believe in that, less than 15% of the population that I take care of and my other hat I wear is the Director of the Intensive Care Unit where I see a number of elderly patients, they don't have a Living Will or a proxy decision-maker, and I think that's a communication and educational problem. So, I think you're on to something there.

(JP) Pat, I think you have a great idea and certainly one maybe ought to ask when you get a driver's

license you sign, they asked me whether or not I'd be an organ donor, they asked me whether I wanted to register to vote, maybe they ought to ask if I'm willing to undergo emergency studies if not able to give consent. I think it's a great idea.

(Caller) Right, I do to.

(JP) Pat, thank you. Thanks for the idea.

(Caller) Okay, thanks. Bye-bye.

(JP) Let's see if we can get to Bill quickly on Bell Atlantic. Bill, you're on WWDB.

(Caller) Yeah, hi doctors. This is fascinating. I've been following several fluid replacement therapies through my career as an EMT and I was a medic for 3 years as well.

(JP) Let's just tell people that an EMT is a paramedic, an emergency medical technician. Those guys, and I use guys generically of course cause it's men and women, are very important in life saving.

(Caller) Yeah, my question is would this study, would you be a) educating providers bringing patients to your emergency room to identify patients, i.e. asking if they're Jehovah's Witnesses or any history or social history that they can provide, to possibly target like we're taught now to do with the TPA, or the other question I had is will this be eventually available for pre-hospital use?

(TS) Well, Bill we have to demonstrate that there's efficacy in this patient population before it can more out of this venue and into the pre-hospital arena.

(JP) If it is effective though, can you see the day when it might be available to paramedics like Bill?

(TS) Absolutely and the benefit of this particular drug is it doesn't require blood typing. Anyone of any blood type can receive this medication, so that's the horizon we'd like to see this agent move in. I think that Bill's point about education, that's what the whole public disclosure is all about and we have various professionals from the police, the EMS, that are involved in that process, so yes, we hope to get that word out and share all of the study requirements with the public.

(JP) Bill, thank you so much for the call. Drive carefully will you?

(Caller) That's why I pulled over.

(JP) Okay. Thanks Bill. We have to take this break. We'll be back to your calls in a minute. We're

talking with about the advisability of doing a study like the one that's under review right now on people in life-threatening situations unable to give consent. My guests, Dr. Thomas Santora, Dr. Pam Crilley, will be back in a second. (Commercials)

(JP) You're back on Medical Frontiers. We're talking with Dr. Thomas Santora and Dr. Pam Crilley. We're discussing a study that is to be done among people in life-threatening situations where they are not in a position to give consent. Dr. Crilley represents the Internal Review Board. She will not let the study go forward, nor will the Board, unless the community expresses some interest in the study. Let me just remind you again, if you're interested in our weight loss program, that's the Meta H Program, you can call right now. The number, 215-TRU-2222. We'll send you stuff in the mail. Michelle at Comcast Metrophone, you're on WWDB.

(Caller) Hi. Yes. I wanted to ask the doctor, there's a couple drugs out now that stimulate the production of blood cells. Could you ever see those drugs taking the place of transfusions altogether?

(TS) Certainly not in the situation that we described Michelle. These patients that are bleeding need massive blood transfusions and those medications take quite some time to be effective.

(Caller) Oh, okay. Thank you.

(JP) Okay. Just to kind of clarify that. You form approximately 1% of your blood cells every day, so even if we could turn on double, triple the rate, you'd still only form 3% in a single day, a single 24 hour period and the fact of the matter is you can lose, what, 40 and 50% of your blood in some massive trauma.

(TS) In fact, most of the patients that we're talking about have lost in excess of 40% of their circulating blood volume, which in the average individual is about 2 liters, which is in the neighborhood of maybe 2 gallons.

(JP) Wow.

(Caller) Could I ask you another question?

(JP) Go ahead.

(Caller) If someone has a pretty good infection such as a staph infection, does that ever cause suppression

of production of blood in any way? Like if they had a.....

(JP) Dr. Crilley, what do you think?

(Caller) an infection in their knee or something like that?

(JP) Dr. Crilley?

(Caller) Could that cause anemia?

(PC) Basically, if you have a serious infection of any type it can suppress bone marrow production which can lead to a lowered white count, anemia, or even a low platelet count.

(Caller) Okay. Thank you.

(JP) Thank you for the call. Jan in King of Prussia, you're on WWDB.

(Caller) I thank you. This is an exciting program.

(JP) Thank you, Jan.

(Caller) Particularly in the area in which I live, King of Prussia, and I'm very conscious of those helicopters going into Allegheny and U of P, all the centers where these accidents victims will receive proper care and I'm just hoping that when you come to the community interests that you're not just going to keep it within the confines of Philadelphia, but will explore how the people in those in whom you are going to contact for this permission or for the okay.....

(JP) Jan, we're contacting folks right now and anywhere that you live if you can hear me, if you have an opinion to express on the study during working hours, call 1-800-PRO-HEALTH. 1-800-PRO-HEALTH and tell them what you think about the study.

(Caller) Oh, that I think is excellent. And, I just want to ask this question, people are taken to a trauma center, they're most likely unconscious, but you're there to save their lives. Would we have to wear a sign saying "we want to go to Allegheny", now I know that is.....

(TS) That's not such a bad idea, though Jan. (Laughter)

(Caller) Well, you know exactly what I mean. You're gonna save lives, are we gonna worry about whether or how you're going to save them.....just save us. Is it going to take a long time? What's the time element on this?

(JP) When could the study start actually? I guess Dr. Crilley's got to give permission.

(PC) Well, we have to have all the elements in place and we have to have permission from the FDA and the IRB, and we have to have positive feedback from the community. And after all that is in place, we can go forward.

(Caller) Do you have it, off the top of your head, how many years?

(PC) Oh no, it's not a matter of years.

(Caller) Oh, that's good news.

(PC) Not at all.

(JP) I would say that if you get 50 or 60 positive calls in the next two weeks that really moves it ahead enormously.

(Caller) That's wonderful.

(JP) I'm going to give everybody else the number, I know you have it already, it's 1-800-PRO-HEALTH and say you want to express an opinion about the blood replacement study. Dr. Santora, you wanted to say something?

(TS) Jan, you might want to look in the area newspapers over the next couple of weeks. We plan to advertise some town meetings that we will discuss this product and the problem of the trauma victim in general, and I would encourage you and anyone you know that has interest in this area to please come out and attend, and if you think of questions like Dr. Posner was saying, please give us a call. I'd be more than glad to answer any question you have.

(Caller) Well, are you gonna be out in our area?

(TS) Well, the exact location of those meetings has not been established yet Jan, but

(JP) Well Jan wants you in King of Prussia. I think you should go out there.

(Caller) Oh, I think he should too.

(TS) I hear you Jan.

(JP) And wait till you see him, Jan. He's awfully handsome.

(Caller) He has so many.... oh how nice. We have so many automobile accidents, you know we live in

traffic.

(TS) I know you do.

(Caller) So, you know, it's going to be important to us. I want to be sure you're going to take care of those of us in the suburbs in your trauma center.

(JP) You make a great point Jan, and I think, you know, I made a little joke there and it was probably inappropriate because this is really a life and death question, and I have to tell you that I personally believe this is a very important study and I hope folks within the community will get motivated to call because some day this study and others like it may save the lives of any of us or our children or our grandchildren.

(Caller) Of course, and when you arrive at the trauma center who is going to care about side-effects...just keep me alive.

(JP) That's right, I agree Jan.

(Caller) I thank you so much. Good luck.

(JP) Thank you for the call. You know, I think that's a really good point, but people listening have got to understand that if they don't express opinions now the study cannot go forward because Allegheny is probably one of the strictest places I have ever been at in terms of protecting people and listening to community involvement. I don't think I've ever been so pressed to justify every more I make when it comes to research as I have been here at Allegheny, and I guess that's you and your fellow Fascists, Dr. Crilley. (Laughter) Protecting everybody from people like me.

(PC) Well, we're trying to protect human subjects. I know that everyone doesn't always agree with us, but we like to discuss it with you because oftentimes you're right.

(JP) I mean, you know, again I'm making jokes, we're on the radio, it's late, we've had a lovely dinner together, but the fact of the matter is I am acutely aware of the fact that just because you're a physician or a scientist sometimes you get so tied up in your subject, you're so sure that your study is important, that you lose sight of the business you're in, and the fact of the matter is you talked about Nazi Germany, but we've seen it happen in this very country and it's a scary business for all of us and that's why all of us feel better when we know there's an external group that is sitting there making sure we don't do anything wrong.

Delores in East Falls, you're on WWBD.

(Caller) Yes. The reason I'm calling you is I know about the artificial blood.

(JP) Yes.

(Caller) One of the area hospitals in Pennsylvania, near Allentown, they have approval to go ahead and give the artificial blood. It was on the TV and it was also in the Inquirer and I cut the article out and they have approval to go ahead and they said they don't need no, for you to sign to get the blood, and also they've been using it for operations now. And, guess what? The patients do well with that and I was glad to know that because being a Jehovah's Witness, I don't accept blood and it would work well for me because sometimes we need surgery and different things.....

(JP) That's right.

(Caller) and, we've been saying all along cut back on the blood, you know, don't use the blood. But now, peoples beginning to say they don't want it either because of other reasons, you know, like diseases and things, you know.

(JP) Delores, may I ask you a question? Do you carry identification in your wallet that you're a Jehovah's Witness?

(Caller) Yeah, I do have one. Now you're making me want to get it out cause I haven't been carrying it and I should because I never know when I'm going to fall in the street or something.

(JP) Right. Because the fact of the matter is if you're brought into any of the hospitals in this area, certainly any of the Allegheny Hospitals,.....

(Caller) Yeah, I'm near there...

(JP) and you have identified yourself as a Jehovah's Witness, you will not be given blood unless one of your family members, you know, or unless you give permission.

(Caller) Yeah, we update it every year. We have a card to carry that says no blood under no circumstances. So, its good to know we can go near Allentown....

(JP) Yeah, go ahead, Tom?

(TS) Delores, it's very good that you picked up on the Allentown situation. The trauma surgeons at

Lehigh Valley are involved with this. This is a multi-center trial, so don't get the idea that's it's only Allegheny University MCP that is involved with this.

(Caller) We know over in Jersey a hospital that has it too.

(TS) Right. Well they'll be about 35 centers across the country and what we hope to do is enroll enough patients so that we can actually see a beneficial effect.

(Caller) You know, I'm to the point now where I thought I would need the surgery, because you know, sometimes you have cancer your blood would drop, and I was praying that I would know somebody to get artificial blood out, you know what I'm saying?

(TS) Right.

(Caller) I know we would have to go to New Jersey and I'd have to get my insurance to approve it. I'm glad now its coming to Allegheny cause that's where my doctor's on staff at, you know.

(JP) You know Delores, one of the hospitals in the Allegheny System, Graduate Hospital, has a whole bloodless care program.....

(Caller) Yeah, I know about that. They sent me something today in the mail. I already had surgery there....I know about that.

(JP) Right. Delores thank you so much.

(Caller) I just want throw it in that we do have it started in Pennsylvania, you know?

(JP) Thank you.

(Caller) Alright, have a nice night. Thank you.

(JP You too, thanks. And let me urge you again, if you have any thoughts about whether you want to see this study done here in Philadelphia, please call us at 1-800-PRO-HEALTH and say you have an opinion about this study. Any final words before we take our final break?

(TS) Joel, I would just echo your point that we really need to have feedback from the community. We're here to serve the community and in this vital capacity we have to have feedback before we can more forward with what we believe is a potentially beneficial therapy for our injured patients.

(JP) So, just call 1-800-PRO-HEALTH during business hours and tell them that you have an opinion about

the study. While you're there you can also ask for our Health Tips absolutely free. We'll be back in a second. (Commercials)

We've been talking to Dr. Thomas Santora, he is Assistant Professor of Surgery, Associate Director of the Regional Resource Trauma Center and Dr. Pam Crilley, Assistant Professor of Medicine, Director of Bone Marrow Transplant Program, but she also is the Chairperson of the Internal Review Board that protects subjects in research. They've been discussing a research study that both of you believe, and I believe, may save lives someday. It is the study of a blood enhancing product really, it's not exactly a substitute, that may save lives of people that come in with low blood pressure secondary to trauma and half of those folks die, almost half die despite best care. They will not do the study without your permission. You can give your permission by calling 1-800-PRO-HEALTH and saying you have an opinion to express about the study, and they'll get back to you and you say yes I'm in favor, no I'm agin, and if there are a bunch of people in favor you're going to let the study go ahead, Dr. Crilley, and if there aren't you're not going let it go ahead.

(PC) That's right.

(JP) Sounds good. Tom, thank you for being here. Pam, thank you for being here.

(PC) Thank you for having us.

(TS) Thanks for the opportunity.

(JP) Come on again and talk about some other stuff. This was really great and let me remind you the number to call, 1-800-PRO-HEALTH. It's also the number for Health Tips.

Attachment 16

000-000074

New Advancements in Trauma Care For Your Community

Each year close to 140,000 people die as a result of injury. In many cases, blood loss is the cause of death.

Research with a new blood substitute is being conducted.

This research may save your life or the life of someone you love.

Allegheny University Hospitals, MCP, in compliance with the U.S. Food and Drug Administration (FDA), is participating in a research study to determine if a blood substitute (DCLHb), manufactured by Baxter Healthcare, which in preliminary studies has shown potential benefit, may prevent the harmful effects of blood loss in severely injured trauma patients.

Emergency medical research presents unique challenges. Most patients will not be able to give informed consent to use this therapy that could potentially help them. For this reason, we are launching an educational program to inform the community about this therapy and its potential benefits to severely injured patients.

In Partnership with the Community

Allegheny MCP invites you to participate in these discussions. Meetings will be held:

- **Friday, April 11, at 7:00 p.m at Devereaux United Methodist Church, 26th and Allegheny Avenue, Philadelphia**
- **Wednesday, April 16, at 7:00 p.m at Falls of Schuylkill Library, Warden Drive and Midvale Avenue, Philadelphia**
- **Thursday, April 17, at 7:00 p.m at C.E. Pickett Middle School, Wayne Avenue and Chelten Avenue, Philadelphia**

For more information, call
*1-800-PRO-HEALTH*SM

ALLEGHENY

Attachment 17

COMMUNITY MEETING
FRIDAY, APRIL 11, 1997
DEVERAUX CHURCH

Sally Hilton - Most of you already know me and thank you for coming out. I am the Director of Community Services at Allegheny University Hospitals and I thank you for being here tonight. It is important that you are here because what you are going to hear about is something that is very important for you to know as much as you can so you can go back and educate other individuals on what is being discussed tonight. I would like to introduce to you three gentleman - Mr. Wayne Vaught who is an ethicist, who is on the Review Board for the study that you are going to hear about, Dr. Thomas Santora and Dr. Vincent Cowell. They will be speaking with you this evening. Please feel free at any time to raise questions that you have or, if something is not clear, please ask them to explain it to you in another way - they are very used to that - I do it to them all the time and they are very comfortable with that. Please feel free to ask any thing you'd like to ask. At this point, I will turn the show over to the doctors.

Thomas Santora - I would like to thank each of you for coming out tonight. I know it is Friday night and it is hard to break away from your families, but I very much appreciate the time that you've given to us because we are going to talk to you about a very important topic.

I am a trauma surgeon and Dr. Cowell is a trauma anesthesiologist. We work over at Allegheny Hospital and every day we see people from this community and other communities that come into our emergency center bleeding and despite our best efforts, some of those people die. In

fact, just last week there was a gentleman from a neighborhood right around the corner from the North Fairmount area who was involved in a minor fender-bender and he got into a little altercation with the gentleman that was struck and the gentleman took out a gun and shot him three times. That gentleman came to our emergency center and he may have been somebody that may have been enrolled in this study that we are going to talk to you about and despite our best effort - four operations and over 100 units of blood cells - that man passed.

We have kids that die every day. Just this past holiday we had another child that was injured on Roosevelt Boulevard who was in a car wreck. She got out of the vehicle to inspect the damage to the car and got hit by another car and was dragged 100 yards. She came into our emergency center. She had a broken pelvis. She had multiple internal injuries. She died on the operating table despite our best efforts.

This is happening in every hospital across the county. Every year 140,000 Americans die from injuries. Most of them die because of bleeding problems. And, in fact, when people come into our emergency centers and they are bleeding and they have low blood pressure, despite our best efforts, mine is trying to stop the bleeding, Dr. Cowell is trying to fill up the tank with blood cells, 40% of those people, 40%, die. That is not acceptable to us and I hope that is not acceptable to you as a community. If we are going to service a community, we have to do a better job, but unfortunately, we have been somewhat hampered in our ability to make improvements in how we can deliver trauma care for a number of different reasons. We are very fortunate right now that the Federal Government has made some changes that allows us to

do research that might in fact prove beneficial and help reduce some of those deaths and improve outcome by allowing us to test new products, new techniques, in the face of overwhelming injury where patients' lives are threatened. We have just an opportunity we would like to discuss with you today.

There is a new medicine that is made from red blood cells that we have been asked to test in patients that present similarity to the stories that I presented to you earlier. People that come into our emergency room with low blood pressure, evidence of bleeding and if those patients get this medication it is our belief that we can reduce the death rate in this population to something that is better than 40%. Now, this is not like penicillin. When penicillin came out in the 1940's it fixed the problem with susceptible infections, people were cured of the infections. We don't have those luxuries today, but rather, we might be able to reduce the mortality or death rate from 40% to 30% and on the surface that may not sound like a lot, but in fact, if 140,000 Americans are dying each year and a 25% reduction in that death rate from 40 to 30% means that we may save about 35,000 Americans each year. And some of those 35,000 might be me or you or someone that we know and love and that is why we are here today - is to talk about having the ability to do this kind of work.

Let me tell you a little bit about this product. It is made from red blood cells. How many people donate blood? Great. Well you know that when you donate blood they ask you a series of questions to try to identify high risk behavior so that the blood supply that we use and Dr. Cowell gives to our patients is as safe as it can be because we don't want to transmit disease,

especially the AIDS virus because it is a deadly virus. Despite our best efforts through the blood banking process, that still happens, occasionally -- one in 800,000 blood units are tainted with that virus. What happens when you donate a unit of blood depends upon your blood type, if it a rare blood type, you may in fact donate that unit of blood but that blood isn't used. It can only sit on the shelves for 42 days. It is not used it has to be thrown away. It has to be thrown away. It is no longer safe to give as a transfusion. Well what this company that asked us to participate in this research did was it took this blood that was going to be thrown away and made another use for that blood. The red blood cells' coating or membrane was stripped away thus making the important internal component of the red blood cell, the hemoglobin that carries oxygen to our cells that is important for ongoing life, it has made that available without the coating. In this process of making available this hemoglobin, it heats that blood and it pasteurizes that blood so that the product that we are wanting to look at is safer than banked blood because in the process it goes through: the entire process of screening that the blood bank does plus when it is no longer usable for transfusion in the process of making of the drug that we are going to study it gets heated and pasteurized. And thereby, killing any virus that might be in that product.

What we would like to do is take this material which has been shown in laboratory animals to increase blood pressure and as we increase the blood pressure in our patients that come in with low blood pressure they are going to deliver oxygen much better to the vital organs and if we can do that and I can operate and Dr. Cowell can give them the fluids necessary to maintain the oxygen supply to the organs that we would have a better shot at keeping people from the

devastating problems that we see on a daily basis.

Unfortunately, the people that we are talking about giving this medicine to often times come in so sick, so injured that they can't tell us, "Yes, I'd like to participate in that study." So the new changes in the law through the Food and Drug Administration, which is the federal agency that looks over how new treatments are developed, has now outlined very strict guidelines by which if the patient comes in with a life threatening problem and the study medication or treatment is more beneficial than it is risky and there is no other way to do the research that once they approved the way we do the study they say that we can do this because in fact the federal government recognizes what we recognize and that is that we need to do better at treating patients with life threatening injuries. But as part of the process by taking away the individual patient's ability to say "yes" or "no" to receiving this medicine they want us to come out into the community and tell the community as a whole what we are planning on doing so that we can get the feedback from you, the community that we serve, to see whether or not you see this as 1) a problem that needs fixing, and 2) whether this fix that we are proposing is a reasonable thing to do. Because if the community does not see both of those things that we ought not to do this.

Vincent Cowell - Dr. Santora has given you a background of pretty much some of the things that we do in our daily job as well as give you some background on this new medication that we plan to use and he has also informed you that the government has said that we can give this without getting prior permission from the patient or the family member and thereby, this is the reason

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Vincent Cowell - Dr. Santora has given you a background of pretty much some of the things that we do in our daily job as well as give you some background on this new medication that we plan to use and he has also informed you that the government has said that we can give this without getting prior permission from the patient or the family member and thereby, this is the reason

we are here tonight. There are two things 1) to inform you about the drug. Inform you why we need to get it, what kind of patients benefit from this drug, and 2) as part of the federal regulation that says that we have to come out to the community and tell the community which we are more likely to be serving what we are doing so that there is no mystery and perhaps alleviate some misconceptions and suspicions which are understandable part of anything you doing to someone without getting prior permission. Again, the purpose is to educate, to inform and perhaps through this education process alleviate some misconception, misunderstandings and suspicions about what we are doing. Pretty much what we are saying is that we have a drug that relatively safe, a drug that we hope through our studies will show that we can save some of these unfortunate victims that all too often, too often, come to our emergency rooms with injuries that are life threatening because they lost a substantial amount of blood. And the one thing that we want to make clear as well is this new drug does not mean we stop doing anything that we normally do. We will continue to do the normal things that we would do to resuscitate anyone that comes in with a life-threatening injury that is bleeding to death. We just select out a population of people which we will choose to use either this drug or use salt water in the normal manner that we would, and, in over a 28 day period look to see if there is any difference in the outcome based upon whether that person received the drug or whether they received salt water. Once we come to terms with the results, we can then decide whether this is a worthwhile drug to use in the resuscitation of people who suffer from injuries to where they are bleeding to death.

Now, we again want to take this further by giving you an opportunity to ask and talk about any

concerns that you have so that we can be sure that we have done an adequate job alleviating any apprehension, any suspicions, about the message we are trying to deliver today.

Thomas Santora - We feel fortunate to be asked to be involved in this study; I say that because obviously both Dr. Cowell and myself and Wayne maybe to a lesser extent believe that this drug holds the promise of being beneficial for the patients that we treat. There is no question in our mind that the problem needs to be addressed by something more than what we are doing.

We are one of 35 hospitals across the country that will be studying this drug. We are the first hospital in the Philadelphia area to get to this point. You may have read the story about the hospital up in Allentown, that was the first hospital in the country to start this drug study. We are the first hospital in the city of Philadelphia. There will be others that will participate in this study, but as Dr. Cowell was saying, what we will do is that when patients come in and they meet the criteria that demonstrates them to have a life-threatening injury, then they will be randomly assigned, meaning that a doctor that is taking care of that patient, whether it is myself or someone else, will go to a box that has a series of envelopes and will pick out an envelope and will open that envelope and decide by the message that is on the inside whether they get the study drug or salt water so that there is not an individual as we are looking at the patient that will say that this patient is such and such so I am going to give him or her the drug. It is all decided randomly. The patient has to meet the entry criteria which means they have a low blood pressure and evidence of bleeding and then that gets them into the randomization process with the envelopes. Then they will receive either 2 coke cans or 4 coke cans full of either the study

medicine or a similar volume of salt water. In and above all the other things that we do. We will give salt water solution to everybody. They may get blood transfusions - both groups. Both groups may get operations and most of the time when people are that sick, they get all of those things. So the difference is going to be one group is going to get standard treatment and a little bit more salt water and another is going to get standard treatment plus the study drug.

Vincent Cowell - On the issue of informed consent we want to make it also clear that it is only in the case where the patient is unable to speak for themselves or a family member or significant other is not present to give consent. If in fact someone is present, the spouse, brother or sister, then we would observe the traditional practice of obtained consent before we would enroll anyone in the study. As well as at any time during the study should a relative decide that they no longer want that individual to participate that we would stop all involvement of that individual.

QUESTION: That was part of the question that I was going to ask, but the first part of it was - When would the study begin?

ANSWER (TAS): That really depends on how well we reach the community. We feel very strongly that we have to have the support of the community that we serve because that is our role and if we can do that, we have this town meeting and two additional town meetings set up and Reverend Sligh is talking about having us come out on Sunday as well. So if we can reach a large fraction of the community that we serve with those meetings, it is our hope that we can

be able to compile all of the information - we have to give this information to Mr. Vaught who sits on the Investigational Review Board that has to believe we have reached the community and the community sees this project as beneficial. That is part of the role that they play and Wayne maybe you can share more on the issue of human subject protection.

Wayne Vaught - I'm not a part of the research study - I don't participate it in - I didn't help plan the research study. I sit on a committee which has been referred to the IRB or the Institutional Review Board. It has another name at our institution which is the Committee for the Protection of Human Subjects - which is perhaps a little more informative name than an IRB. These committees have been set up all across the country at any institution which received federal funding - whether it be Medicaid, Medicare, funding from the National Institutes of Health to do various types of research or any institution which receives that type of funding has to adhere whenever it does research according to certain federal regulations which have been established to protect human subjects. These regulations were established in the early 70's and one of the main requirements of those regulations is to protect subjects from any type of research risk, any type of harm that can potentially come from the subjects participating in those research projects and to guarantee that subjects give their consent to participate in research so that researchers just can't go out and say, "Today I am going to do a project. This is what I am going to do and I am going to gather up some subjects and experiment on them." That type of thing can't happen. Anytime someone wants to prepare a project like they have, they submit to our committee which will review that and we try to look through their document to make sure that certain things meet certain criteria to make sure that it is consistent with the federal regulations and one of those

requirements is generally an Informed Consent Form which must be part of every research protocol. What is being asked here is that in certain circumstances for them to waive that consent. So that we have to take that very seriously because we do not want people to be harmed by research. We want to protect the rights and the interests of the research subjects so that our committee will evaluate their project and will take into consideration feedback that we got from the community, from you, that will all come to our committee. We will review that, we will review the protocol, we will see if it is appropriate. You can't just waive consent. There is certain criteria which have to be met before you can waive consent and one of the research criteria is that informed consent cannot legitimately be gathered and the type of patients that will be coming in - you can't get consent from them and the need for this particular product is so great that it is usually impossible to get consent from a family member or someone else. So given that there are those federal guidelines we will make sure that it falls out, we will make sure that there are no foreseeable risks that we can see that haven't been taken into consideration. And then we give approval for a research project to be conducted once we have guaranteed that all of our concerns have been met and in fact protection of human subjects can reasonably obtained in the research protocol.

So that is my responsible as a member of the Institutional Review Board. So I don't participate in their study. I just evaluate their study making sure it is consistent, making sure that there are certain ethical requirements and legal requirements and then we give permission for them to go ahead and do the research.

QUESTION (woman)- I had an operation - I had a bleeding ulcer - when I got up there I had to ask them for blood and sometime I have a lot of burning in my body and I want to know what blood that you all gave me.

ANSWER (TAS) - This came up at a number of meetings. Blood transfusions are not without risk. I think that Jehovah Witnesses are probably the most vocal about some of the risks that are associated with blood transfusions. Some of the things that people relate to prior transfusions such as having change in personality or this burning sensation that you are referring to it's hard to attribute that to the blood itself, but rather especially the change in behavior may in fact be related to the reason why someone needed a blood transfusion. They may not have gotten enough blood to their brain.

(woman) I have high blood pressure - would that cause that?

ANSWER (TAS) - I don't know about that.

QUESTION: I have a question in reference to community, if I do have a large crowd, but could you possibly get a lot of the information about to the community - How would you determine whether the outreach what was the suspect at various meetings and at this particular community and the other thing - How would you determine to make sure that the community was aware? Ok, we had enough community outreach. Ok we will approve or ...

ANSWER (W.V.) - It is fairly difficult and in some ways subjective, but therefore following the requirements of the federal regulations and one of things is documenting that you signed in when you came her tonight. The information is being recorded. Questions are being recorded night. We will have access to those. There was a radio show that was done and potentially brought our audience of people who will be listening to that. We just can try to estimate Does it appear and Does the information, the data that they are going to bring back from these types of meetings and the signatures that we have addressed the question and concerns. Does it appear that they in fact reached the particular audience that was necessary to meets those guidelines. So we are just going to have to evaluate what comes in with what we are required to do.

TAS - Along those lines I think what Mr. Vaught said is absolutely right and there is no answer to that question. This is the first trial that tests these new federal guidelines. Ok, so what might be applicable in Philadelphia is not necessarily the same set of guidelines that would be applied in Los Angeles for example. So, one of the things that we are planning on doing is that we convened a group of community leaders, about 12 individuals, were asked to come to the hospital and they gave their time for this project to hear what we had to say. Basically the same presentation that we are giving today and we asked those folks, Officer Dean and Rev. Sligh were two of the individuals on this council - "How do we reach the community and how do we communicate with the community." We used input from that council to arrange these town meetings.

V.C. - For you get to the point where they won't realize that are being involved in a study or

a project that they might not want to be involved in and what we want to do is a couple of things 1) also look at the other side and I'm sure that everyone in here is aware of that there is something that is in the news right now is that President Clinton has elected to issue an apology to an experiment that was done not too long ago in Tuskegee where in fact a group of black folks were denied therapy to see how the progression of certain disease would go. So in fact we have two sides of who to look at this. And either include or exclude people from this study. And so, this approach we hope will do a couple of things 1) is through education and through public disclosure is let people know exactly what is going on and have an opportunity to be involved in the decision making of what goes on and realize that what we are doing is that we are trying to save lives of those who are at most the most vulnerable point of loosing their lives, I'm sure that most people feel that sometimes you might feel one way sitting and hearing about it but if a loved one is facing a possible critical injury you probably would want everything possibly done to try to help save that individual's live. And so what we are trying to do is again is trying to reassure everyone through this communication that of what we are trying to do is give you an opportunity to ask your questions and hope to clear up an misconceptions that there may be.

QUESTION: What mixture of the community is on the review board?

ANSWER (W.V.): The IRB is made up primarily of a variety - sort of disciplinary people from within the institution. We do have a community representative who sits ont he IRB as well who is not a physician - is just a person who lives in the neighborhood and she reads through the protocols and participates and voices concerns that she feels would be appropriate for the

individuals she is attempting to represent, which is the people that live around here. So there is a community representative, but mostly it is professionals at the institution, scientists or clinicians or other types, myself being an ethicist.

Tape 2 - Side A

QUESTION: .... What are the benefits of this drug and ... what kind of

ANSWER (TAS): We absolutely agree with that. Right. Right. Sure. Let me put it into perspective. I'm going to answer your question and I'm going to try and touch every point, and if I don't if you can just remind me. But before we were in the process of being asked to participate in this study they said "How many people would you at your trauma center take care of that might fit into this situation of having life threatening injuries and having that from bleeding." So we did an analysis, we keep records at the hospital of all the trauma patient that we see - and we see about 1,000 patients a year that come through the trauma center. Not the ER because the ER sees many more people, but just the patients that are admitted to the trauma service which are surgical patients. Of those 174 patients fit this criteria in three years. So we are talking about on average somewhere about 50 patients a year. So many 3-5% of our patient population and then to try to find out where in our community these patients lived prior to their injury, we broke that down by patient's addresses and their zip codes. And I'm to tell you that 52 of those 174 patients came from North Philadelphia.

QUESTION (man): where did you get those numbers?

ANSWER (TAS): Medical College statistics. So that's why this is an important community for us. It's your brothers and sisters, mothers and fathers, nieces, nephews that are being injured

and coming to our hospital severely injured and life threatened. That's first and foremost. The beneficial aspects of the drug - It increases blood pressure. And as a hemoglobin it carries oxygen. Oxygen is the most important nutrient for every cell in our body. It sustains life. So by increasing blood pressure and carrying oxygen we can support life until I can get the bleeding controlled and as Dr. Cowell is tending to maintain the vitality of all the other organs while I am working, he is working, this medication hopefully will allow us to diminish the bad effects that bleeding cause. Most of you have probably have heard of the idea of the "Golden Hour" after injury. If you can't improve the blood supply to vital organs within an hour after somebody is injured, they are going to have a bad problem. They may not necessarily die, but they are going to have a bad problem. So this medication holds promise because we can improve the blood supply and carry oxygen to the tissues. And it tends to normalize blood flow to those vital organs.

Now, are there side effects? Absolutely. In fact, raising the blood pressure is a side effect. What we have seen is as soon we give the drug. I mean instantaneously, the blood pressure begins to rise. It normally rises about 35% above where we start. OK? So if we are talking about somebody that has a high blood pressure to begin with then we may make a problem making it even higher. But remember the people that we are talking about have come in with low pressure. They may in fact be high blood pressure patients or hypertensive patients, but when they come to us their blood pressure is low, and, in fact, somebody that has a high blood pressure normally that has a low blood pressure is going to have a whole lot more problems than somebody who has low blood pressure but has normal blood pressure normally. So just raising the blood pressure is a side effect but in this particular population of patients that

is going to be a positive thing. Might it be negative, it might be, in the fact that until I can get control of the bleeding, raising the blood pressure may in fact cause more bleeding. However, in animal studies it doesn't seem to do that anymore than the salt water solutions or the other resuscitative fluids that we normally use. But that may be a problem that's why we have to test this. The other side effects that seem to be fairly common with this medication is that it tends to transiently create yellowing of the skin. Because the medicine resides in the skin until it is removed from the body it will discolor the skin. You may hear the term "jaundice." When we talk about the term jaundice in the medical sense it is usually because of a problem with the liver, but in patients that have received this medication, their liver is fine, they just have this yellow discoloration, because when this medicine is in the skin, it is yellow. It is red like blood and some of this material is filtered in the kidney and it can turn urine transiently red. The blood pressure that we talked about, the elevation in blood pressure, that also is transient. So there doesn't seem to be any long-standing effects of this medication and, in fact, the body eliminates this medicine within 48 hours.

QUESTION: How long does the yellow color stay?

ANSWER (TAS): The yellowness goes out of the skin at 48 to 72 and the longest its been around is 5 days.

QUESTION: Is this to be a "last resort measure"?

ANSWER (TAS): Well Ma'am, I wouldn't call it a "last resort." I would say that what we do

today we really haven't changed our approach to the severely injured trauma patients in 20 some years, really. We are looking for new ways to improve outcome and I come back to the problem and that is 140,000 Americans die because they bleed to death and when somebody comes in and their blood pressure is low from bleeding, 40% of those people despite Dr. Cowell's best efforts, my best efforts, the emergency ambulance crews that scoop the people out of the street and bring them to our emergency room as fast as they can. Despite all of that, 40% of those people die and who are those folks. In this community, they are young black males.

QUESTION:

ANSWER (TAS): No, No, No. If they meet the entry criteria of having a low blood pressure from bleeding they will be enrolled in the study. They may not get the drug, they may get salt water, but they may get the drug.

QUESTION: Age

ANSWER (TAS): There is no cut off of age on the high end, there is on the low end at 18 because the issue of consent from parents and all. Did I answer all of your questions?

QUESTION: I was wondering if you ???

ANSWER (TAS): No it does have drug effects. It carries oxygen and it tends to normalize blood flow and it does that by combining with an element that happens to adversely affect the drug vessels and hemoglobins of all kinds scavenge up this material that tends to dilate blood vessels so that it acts as a drug. It has drug-like effects. You can call it a medication. You can call it a drug. It is a blood product. Okay. I'm not going to try and hide behind anything.

QUESTION:

ANSWER (TAS): Taken away. The coating of the red blood cells, the cells that we have in

our bodies is striped away from this medication. Red blood cells have a shell around it. You can think of it as an egg. The cell membrane is the shell and then you have the white of the egg, that's the fluid through which the yellow part, the yolk, is hemoglobin. And what this company has done is that it has stripped away the shell and it has removed the white of the egg and is left with the yolk, the hemoglobin, which is the important part of our red blood cells and, in fact, whether you are Afro-American, Caucasian, Native Indian, Asian, or any denomination, we all have the same hemoglobin. There are some different hemoglobins, like sickled hemoglobin and that sort of stuff, but the basic hemoglobin is the same. So the thing that makes us different is that the coating of the red blood cell has blood types, markers, on it so that if I wanted to get a blood transfusion, I would have to have my blood typed and I can only receive red blood cells that have the same type as mine because if I got another type my body would react violently against that. But by removing that coating that contains all those type markers, the hemoglobin can be given to anyone.

QUESTION:

ANSWER: Right. When I say it is a drug, it has drug-like effects. I think it is just a symanic thing.

V.C. - the company refers to it as a blood substitute. For simplicity, some people call it a drug. Some people call it blood substitute. But it is just a matter of symanics.

QUESTION:

ANSWER (V.C.): One other thing I just wanted to clarify. People dealing with the issue of blood transfusions do it for different reasons. The Jehovah Witness, in fact just to make it clear, do that for a religious belief not because of the fear of AIDS, hepatitis and what not. Other people make choices of blood transfusions for fear of transmission of diseases. Other people make decisions about transfusions just because of the principle that if they don't have to have somebody's blood, they don't want it.

QUESTION: Is there an allergic risk?

ANSWER (V.C.): With this drug, none. Because as Dr. Santora just explained the part that causes the allergic reaction has been removed. There is just the hemoglobin part of the blood that would be given. Blood is a product that have many constituents. It has white blood cells, red blood cells, it has platelets that cause bleeding to stop by plugging in holes. It has much hemoglobin. The purpose of hemoglobin is to just carry oxygen. The blood does many things - it carries sugar, it carries protein, it carry enzymes. Again, this substitute doesn't do everything blood normally does. All it does is carries oxygen which is a vital part of the immediate resuscitative efforts. What we are doing is not giving you something that is going to save someone's life for the long haul. This is something to try to make an impact during that first hour that someone comes in and may make the difference of whether or not we get the chance to continue a person's life beyond that immediate point were we see them in the emergency room and get them to the operating room and by the time we make a decision to give you blood in the emergency room, you best believe you are in trouble.

QUESTION: What gets a patient qualified for this study?

ANSWER (TAS): There are 2 - low blood pressure and evidence of bleeding. Those are the only criteria.

QUESTION:

ANSWER (TAS): That is on your way out Ma'am.

V.C. - When you get injured and a major vessel is open and you start to loose blood your body is normally able to try to cope with it. It tries to stop the bleeding. Your body starts to clamp down on the vessels to try to keep the blood pressure up. The point of trying to keep the blood pressure up is that it drives blood to the vital organs - the brain, the lung, the kidneys. Once the body has done all it can, then what happens is that the kidneys no longer get that blood, so then you start to have kidney problems. The liver no longer starts to get blood, then you'll have liver problems and the brain no longer gets blood, you start to loose neurons upstairs and what we are trying to do is get a product that will at least provide those organs with oxygen until we can get the hole fixed, until we can get you some other products that the blood normally carries and one that coagulates, and stop the bleeding and plugs the holes so we can give you factors that carry proteins, nutrients and other things. Again, it is a way to help us take care of you in the acute or the critical "Golden Hour," one hour phase immediately following the time that we get you into the hospital and try to take care of you.

QUESTION: Will other patients be able to receive this blood substitute, for example a woman who has given birth and is losing a lot of blood?

ANSWER (V.C.): It may eventually may get to them, if in fact that we find that this drug is of benefit and, in fact, helps to save lives in this situation. Again, what we are doing here is not a whole lot different that any drug that we use today. Every drug, every product, medical product, or whatever has to start off somewhere. What happens is that somebody discovers that this works to take care of a problem. Then they try it out on animals. Then they present it to the government and say "Look at our results. This is what happens when we use this drug." And the government has a big committee, and it is much bigger than his (our IRB), but very similar to his, that makes a decision whether they think this drug is going to be helpful or not in the care of people and they give their approval and then this drug comes on the market. What the drug company has to do before it can do that is that they have to show proof that the drug works in animals and it has done some research in humans. Alot of trials on humans go on in Europe, India or in other places that don't have strict FDA guidelines and things like that. So they bring the data back from over seas and say look at what happened to people over there, it worked. Sometimes the public hears about something that is working overseas and the public is the one that knocks on the government's door and say we need this drug. An example would be the AIDS patients that find out that they are using a potentially beneficial new drug in Europe and the FDA is dragging their feet and they are dying. We need this drug. There is a series of steps or protocols that must be completed before a drug is finally approved and this study is one of such trials. The drug company now is saying to us - we want to include in 35 sites around the country - we want to make that point clear to you - this is not just on inner city people, this is in the suburbs, like Allentown. This is not only on people getting shot. These are people who are involved in car accidents, who fall off tractors, get hit with baseball bats.

However you can put a hole into somebody. These are people that might be involved in the study around the country and once the results come in from these centers the company can go back to the government and say this is what we found. If it looks like this drug helps, then the FDA says go ahead and use it. If it doesn't look like it helped much at all or if it hurt people, they will say go back to the drawing board.

TAS - To amplify on that - this drug has been studied in about 350 people over the last four years and the process that the food and drug administration goes through is that they have to demonstrate that the medicine is safe before they can allow the company to increase the dose. So what they do is that they start giving the medicine or the substitute or whatever you want to call it at a low dose and then increase the dose to see if it has any adverse effects on people. Those trials have already been done to demonstrate that at the higher doses, this medicine is safe. So now what the drug company has to show is that not only is this a safe drug, but it is also something that can be helpful and if it can be helpful in patients that have low blood pressure from bleeding due to injuries. If efficacy is shown in patients with traumatic hemmorhagic shock, then you can use this substitute in women in child bearing that have low blood pressure because their uterus is bleeding for it doesn't really matter what the cause of the bleeding that creates the low blood pressure is. If the drug is effective it will be effective in that population. So that's the hopes that this drug does in fact realize the potential that we believe it has then it will come on the market and any doctor can use it in the appropriate circumstance.

QUESTION: Will other trauma centers in Philadelphia do this study?

ANSWER (TAS): There are now five trauma centers. There used to be six, but we combined with Hahnemann. Temple is one. Temple is one the docket for this study as is Einstein. The people at Jefferson are talking about it. The people at the Hospital of the University of Pennsylvania are talking about it. But we are the first of the trauma centers in the city to get to this point.

QUESTION: Is there any information on the benefit of this substitute in people?

ANSWER (TAS): Well again, this process is moving along fairly rapidly. Some of that data is in the process of being written ... so in other words, these papers may be, some are written, but some are in the process of being written.

QUESTION: Is there information on the use of this substitute in bleeding trauma patients?

ANSWER (TAS): There is certainly the animal studies that have shown benefit especially for the shocked animals; for people that are in shock -- that information doesn't exist because that is the trial that we are trying to do right now. So there is some work that has been done in cardiac patients for example, that this medicine, or blood product, or whatever you want to refer to it as, has been shown to reduce the need for blood transfusions after open heart surgery. This medicine has been helpful for patients with kidney failure on dialysis. It tends to improve the blood supply to the kidney and it has been of marginal value in patients that have strokes; the idea here was if you can increase the blood supply to the brain at a time when it was most vulnerable maybe you can minimize the effect of the stroke, but unfortunately to date, that has not been shown to be beneficial.

QUESTION: This information about the use of the substitute in people doesn't exist?

ANSWER (TAS): I said that stuff is not written in the journals yet. It has been presented at professional meetings but it has not been in print yet. About the efficacy of the blood product. Again the safety of the blood product has been shown and the beneficial effects in laboratory studies that have prompted the human trials are in print and I think that Sally has that material - Did Sally not get you that packet - She has it - absolutely.

V.C. - One other point I wanted to make to is that in terms of being able to evaluate whether or not we did our jobs in terms of presenting to the community. I want to emphasize and I wanted to do this a little earlier is to thank each and every one of you and applaud you for your community concern and interest in showing up. This is two way street, we must make an honest effort to get this information out and try to make an honest effort to let each and every person that cares about it, know about what we are trying to do here. But there is also a community responsibility that if people have a concern, then it probably worth the effort of trying to show up and be a voice as the process is evolving as apposed to be a voice after something has happened. Rev. Sligh shared with us that it is probably not a good plan to communicate information when we have a full house when there is a crisis after the fact; what we are trying to do is get people to come out and be a part of what we are trying to present here so that we can perhaps shed some light on some misconceptions and to have an opportunity to ask questions and participate. For the people who didn't make this meeting, we understand that people have things to do, it is Friday night and people get off of work. We are holding two other sessions - one which is not too far from here, Pickett School and another one at East Schyukill Library.

We again are trying to get that information out though word of mouth and newspaper advertising and someone even suggested that maybe the Mary Mason's show. In any rate, we encourage you all to ask anyone who has a concern to perhaps come back to one of the other meetings, Rev. Sligh has made his congregation and church available this Sunday. You are more than welcome to feel free to call me, Dr. Santora, or Sally or anyone in communications here to voice some concern and get some questions answered.

QUESTION: You said that you will pull an envelop out of a box to see who gets what and do you know how many people will receive the substitute vs.the salt solution?

ANSWER (TAS): No, there will be equal numbers but they may not be equal at our hospital necessarily. What we are going to do, we expect to enroll about 20 patients in either 12 to 18 months and they will be sequentially numbers 1,2,3, all the way to 20. The first patient who comes in gets envelope #1, the second patient #2, and we may find that out of that 20 it will say the study medicine 11 times or 12 times and it will say that salt water 8 times or maybe vise versa.

COMMENT: Then it won't be an equal number.

TAS: Well I don't know. It may be. But what they're going to be is over the 35 centers that will do this study across the country, there will be somewhere in the neighborhood of 850 patients enrolled and about an equal number will receive the salt water in addition to the standard therapy verses the blood substitute and the standard therapy.

COMMENT: Okay, then in other words, the number that's going to come out will be equal?

TAS: Yes. Yes. Right. But we don't know what those envelopes say until we open them.

That is the point we are trying to make.

QUESTION: How would patients get into the study?

ANSWER (TAS): Well, first of all you have to have low blood pressure and evidence of bleeding. Those are the two things. If you came in as the family, we would approach you and say your loved one meets the entry criteria for this study and we would like to enroll him or her in this study and you can give consent for that individual.

COMMENT: Could someone request the substitute?

TAS: No Ma'am. No it would not. The reason that studies can't be given like that is that would enter bias into it because again, this drug has potential to be beneficial because it increases blood pressure and it carries oxygen. However, to be very honest, as I mentioned as you increase the blood pressure that might cause bleeding, more bleeding and maybe that will have a detrimental effect, it didn't in animals, but we're not animals. So even though most things are analogous as you go from animal studies to humans, but we don't know that for certain. So we can't come in with a preconceived bias. It has to be a random process.

QUESTION: What will the patients who don't get the substitute get?

ANSWER (TAS): Usual medicine plus a little bit more salt water. So in other words we are doing the same thing. In other words we are doing the same thing. In other words we are going to have two teams of people taking care of the patient. There is going to be the trauma surgeon and the anesthesiologist and then will be another team that deals just with getting this medication in the study group. So that there is not any bias by anything, we try to do the same things in both groups except that in one group there is going to be an equal volume of salt water and the other group an equal volume of the blood substitute.

QUESTION: How many people will be involved in this study?

ANSWER (TAS): A number of patients? Yes. Yeah, there are ways to determine how many people you need to enroll in a study dependent upon what you expect the medicine to do and that had been done and to show a 25% reduction in the death rate in the patients that received the study medicine versus standard therapy essentially, they need 850 patients.

V.C. - that's not just from our center.

TAS - Right. The expectation is that the majority of trauma centers will be like ours, busy so that they can enroll 20 patients within about a year to 18 months. So that is the expectation.

QUESTION: Will the information from the study be available for review?

ANSWER (TAS): As a matter of fact, as patients are enrolled, that information is going to go to an independent safety board. That is another one of the safeguards for the human subjects that will be enrolled in this project. This safety board is made up of people that aren't the investigators, like Dr. Cowell and myself, and they are not the sponsor, they are not the federal government, but it is this independent group of scientists who will look at the data as the data comes in and after about 400 people are enrolled, they will look and compare if there is a difference between the people that received the study medicine versus those that received standard therapy and a little bit more salt water. And if that number of patients shows that there is a marked improvement in survival after the study medicine, they will stop the study right then and go to the FDA and say that there is no reason to continue to test this because it is no longer ethical. It's like the Tuskegee thing. If we demonstrate that we have a beneficial treatment it would be unethical to not make that available to everybody who comes in under these circumstances. Likewise, if that same safety council found that the study medicine was creating

a worse outcome, it would stop the study and tell them there is no way the study is being continued and you are going to have to go back to the drawing board.

QUESTION: Will this information be made available to us?

ANSWER (TAS): Well, I think that it hard to do that because it may be that all of the patients, God forbid, all of the patients that get enrolled in our site, they all die regardless of what they get, regardless of what happens. And up in Allentown they all live regardless of what happens. And that is just sort of how it happens. We know that these people are so sick that we don't expect their mortality to go from 40% to 0. We don't expect that. Realistically, that is not what is going to happen. But hopefully we can save some of these people. We can reduce their mortality from 40% which we know it is and it has been that way for years in this population to 30%. OK? And again, that may not sound like a lot, but that 25% reduction in the death rate over the entire United States amounts to 35,000 Americans each year. So that is a big deal. But, can we look into the feasibility of doing that. Sure we can do that.

Well you know that Sally Hilton had suggested that we develop a trauma liaison group with the community and I think that is a fabulous idea because again, I think it is important that you all understand that this isn't the fix to the problem that I see and Dr. Cowell sees every weekend or every day that we are on duty in the emergency room. This isn't the fix. The fix is stop the drunk driver behind the wheel, take the gun out of the, especially the younger kids hands. That's the fix. But until we can get to that point, we need to have better tools to work with because I will tell you it is real frustrating coming in day after day and seeing young people, especially young people being picked right out of the prime of their life, the most vital part of our community, despite our best efforts. We gotta do a better job.

QUESTION: Woman - I have trust in this doctor of what he is saying because he is the one that saved me when I went up there, I had lost so much blood I was loosing consciousness. I had to be rushed into the emergency room and they started working on me right away. He was there to with blood and all that.

ANSWER (TAS): There is a contact number that you can call 1-800-PRO-HEALTH and I have tried personally to contact everybody who has called the number and I will do my best to continue this practice. But again I think that if it is possible to get as many people that you can talk to the next couple of meetings, because realistically what I hope that you get out of this meeting is that we don't have a hidden agenda, people are dying left and right and we need to try to fix that problem and this is one potential fix and the sooner we can get to this, the sooner we can start on our mission. So we can get caught up in this progress trying to reach out into the community and I think that it important. However this project turns out, we are doing the right thing and we need to continue working with our community. That's what we are there for is to serve the community and I think that if we can get a larger group at the next couple of meetings and a real good mix that we can have interaction and we can bring that information back to the community council and then on to Mr. Vaught's group and we can move forward with this process.

QUESTION: You sent out information about this meetings?

ANSWER (TAS): Yes Ma'am. We have sent out fliers, ads and specific letters of invitation to these meetings. Yes. That was one of the reasons and one of the expertise that we got from our community council. We tried to identify how best to reach the community and we got

contacts from various church members and church leaders, block leaders and we sent them personal letters of invitation to these meetings and again, I'm not discouraged. I'm not discouraged with the turnout of this meeting. I think that the Reverend is right on the nail, as I'm sure he is most times, people don't respond unless there is a crisis or they have strong feelings one way or another and one can look at this saying we made this information available and you as members of the community must have felt strong one way or another to come and listen to what's going on. You need to voice your opinions just like Ralph said. We really need to know how you feel about this problem, this potential research project and anything else that might impact how we take care of you as our community.

QUESTION:

ANSWER (V.C.): Again, we were just trying to share with you an honest effort to try to help some people that far too often have been overlooked. I couldn't begin to stand here and tell you how it breaks my heart to see the unfortunate situations that come across my work. That's the real problem. But we can help some people. He was just saying that a young man is no longer safe; we see them come to us at 10 or 11 years old with pockets full of drugs and seriously injured.

V.C. - Any other questions before we wrap things up? Concerns? Comments?

Attachment 18

Second Town Meeting at Schukyll Falls Library

Dr. Sokil is here to be able to answer any questions that you may have about the institutional commitment to the protection of people that are involved in research studies at our institution in particular.

My name is Thom Santora and I am one of the trauma surgeons over at AUH/MCP. Vince Cole is one of my associates in the Department of Anesthesiology. We are coming to you today to discuss an opportunity that we have to help the patients that we see on a daily basis. As a trauma surgeon I am called down to the Emergency Room very frequently, just about every night that I am on call, to try and evaluate and put back together people that have been severely injured. For example, not long ago an individual from this community was walking along the railroad tracks down here and had his walkman on and did not here the train coming and was struck by the train. This fellow came into the Emergency Center, as you can imagine, he lost that battle and was pretty badly injured. When he came in his blood pressure was low and he had evidence of bleeding into his belly cavity. He would have been a candidate for this study. Fortunately for him we were able to get him to the operating room and get him patched up, but that gentleman spent about 3-1/2 weeks in the hospital and required two operations to get that done. We had another child not long ago that was involved in a motor vehicle crash on Roosevelt Parkway. A minor fender bender got out of the car and in fact was truck by another vehicle

and dragged 100 yards down the road. This child was brought in to the Emergency Room with barely a pulse. We were able to get her pulse back and take her to the operating room where she had extensive intra-belly injuries and a badly broken pelvis and despite our best efforts, this 17-year old girl died on Christmas Eve. These are the tragedies that Dr. Cole and I see on a daily basis and this is just a couple of examples of what could be said of 140,000 Americans every year that dies as a result of injuries. It happens to young people, old people, people of all race, religion, creed, you name it. A vast majority of these folks are in the prime of their life and, in fact, trauma is the leading cause of death for persons under the age of 44. So this is a cataclysmic problem and right now when patients come to our Emergency Centers and their blood pressure is low from bleeding 40% of those people die despite our best efforts. 4 in 10 patients despite Dr. Cole filling up the tank and me trying to get control of the bleeding they die. That is unacceptable to us as people who see this on a daily basis and I would hope to think that this is unacceptable to the community as well. That is what we are here to talk about; is the opportunity to change some of those numbers. We were invited to participate in a research study of a blood substitute that has been shown to have promise to improve blood pressure and improve oxygen supply to injured patients. Oxygen is our most important nutrient that keeps ourselves alive and we have been taught through medical school that injured patients have 60 minutes, which is called the Golden Hour, after they are injured by which if we could fix the blood flow to vital organs we have a

fighting chance to get a patient through even severe injuries. The hope is that with this research study we will use this blood substitute in addition to the standard treatment that we use today that is the same in every trauma center across the country, but we want to look at this medicine that will be given shortly after a patient arrives in addition to the standard treatment to see if this medicine can improve the blood supply during that Golden Hour so that we can potentially get more people to survive. Just as I was talking to a man in the back, this medicine is not expected to be the same results as we saw in the 1940's with Penicillin. When Penicillin first came out we gave it and peoples infections were cured. We do not expect that with this medicine. There are going to people that are going to get this medicine and they are going to die anyway because there injuries are too severe but what we are hoping is that it will reduce the number of people that die by 25%. Say instead of 40% mortality in the standard treatment we expect to see about 30% mortality in the patients that get standard treatment and this blood substitute. That may not sound like a whole lot but, in fact, if we talk about 140,000 Americans and we can reduce the mortality from 40% to 30% we may be looking at saving upwards about 35,000 Americans every year and one of those people may be God forbid somebody that is near and dear to our hearts. That is really what we are trying to do is to service the community. We as medical people that see this side of our community activity see this as a huge problem. It is killing our young people. Is this the fixed of the problem that we see on a daily basis, absolutely not. We need to take the guns out of the hands of kids, we need to

take the bottles and the drinking out of the people behind the wheel, that is going to fix those problems but until we do we as people that take care of injured folks need to have better tools to take care of these folks.

Another person:

To explain a little bit more about ??? is that the reason we are here is that this blood substitute product called ??? is a substance that has been produced by a company called Baxter Health Care Corporation. This blood substitute has already gone through some experimental research with animals and has also had some human exposure as well although it has not had the kind of exposure in the patient population that we are trying to familiarize you with. What has happened thus far with this research is that the government has sanctioned us to begin trials with this research. If we can communicate with the community to allow them to participate with a voice and feedback information knowing what we are doing and giving us some feedback as to what they feel and what they think about this process, about the research, about the possibilities of being affected by what we are doing. This blood substitute product again is primary purpose is to carry oxygen to the vital organs so that the cells receive the nutrients from the workup of this blood substitute may perhaps a better chance of surviving the critical period in which the person is literally fighting for their lives. The government has allowed us to use this without having to get consent from the individual because of

the circumstances under which most of these patients come to the hospital. Most often the patient comes to the hospital and may not be accompanied by loved ones or may not be accompanied by someone that is in the position to give consent to us care for the individual and quite obviously the individual themselves are not in the position to give their consents. In the event that someone is with the individual that is in the position to give consent, we would follow the normal protocol that follows in any situation ?????

This being a husband, wife, child, etc. ??? Tape gets lower and I cannot here what he is saying.

Question: ??

Thom: Every case. Right, but the problem we are faced with is that trauma is unpredictable. We could walk out that door and get hit by a car and unfortunately that happens all to frequently and then the patient is brought to the Emergency Room with life threatening situations and there is no one accompanying that patient. However, we will inquire whether or not there is some there, we will look through their pockets to find out who this individual is and try and contact a love one as we do now to let them know what the situation is and under those circumstances ask if they would participate in this research trial.

Question: ??

Thom: At this point in time the federal government in this three year process has put a moratorium essentially on doing research of any kind in the face of emergent circumstances because when people come in either with heart attack, Dr. Sokil's other hat is that he is a heart doctor, and when people come in having a heart attack there are certain things that have been put on hold because that patient really can't give an informed consent because they are too concerned about dying. So in a situation very analogous to the patients that we take care of under these circumstances. So in three years the federal government working with scientists, ethicists, lay people have developed guidelines that just went into effect November 1, 1996 that stipulates that if you have a life threatening situation and you have a study treatment whether that means some medicine, a blood substitute, some kind of operation that has shown more benefit then risk and that there is no other way to do the research trial and that the federal government has looked at the exact plans for the research and have found those to be acceptable and the group that Dr. Sokil heads at the individual hospitals has gone through the same process in looking at the protocol the exact steps that the researcher will do if those two groups are found appropriate then a patient can be enrolled with an exception to informed consent. The additional safeguards for the subjects because the individuals often times won't be able to give consent because they are not thinking clearly because their blood pressure is low is to go out into the community as we are doing now and to try and reach the people that potentially may be subjects for this research, God forbid anyone in this community, but the

point of the matter is trauma is completely unpredictable and if the community is aware of what we are doing and they have the opportunity to come to us, hear more information, voice opinions and concerns and essentially the sense that we get and Dr. Sokil's main purpose here today is to get some feedback from you as a group. If you see this is beneficial and you see the problem as life threatening then we would proceed. Now if the community said I do not see this as a problem meaning that it is okay that 40% of people that come in like this die, I do not see that as realistic, but if that is not perceived as a problem or just for whatever reason don't like the idea of the research or you don't like the idea of having individual patients rights taken away then we are not going to proceed. Let me speak about the rights of the individual. I for one will always seek love ones to tell me what to do and help make decisions. That makes me feel better. I know what I would do for an individual if I had the only say in thing but what I am saying does not matter for the individual patient. That patient is the primary decision maker and, when that patient cannot speak for him or her self, and it is the family that knows that individual best they should be able to speak for them and that is how we do business. However, I also believe that the most sacred ?? is life itself and the way I see this is that 40% of these people that come in that fits this bill are going to die. So they lose that right to life and with this product I might be able to save some of those people. That is the right that I think gives us the right to proceed with this exception for informed consent but we have to do it properly.

Question: ???

Thom: First of all the study is not continuing it is just being started. The way that the federal government and the FDA in particular oversees a drug development it has to show that the drug is first off is safe and it gets to that point only after it has been shown to be effective in laboratory animals. So if the drug is not effective in laboratory animals then there is no reason to test it in humans because why would anybody regardless of how safe it is want to use something that is ineffective. Animal laboratory studies are important because what efficacy it is shown to various treatments are often times equivocal to the human. So that if we were develop a model where animals have bled given this material which has been done it has shown that the animals that received this medication lived whereas the other animals that do not get the medication died. There is a difference between those two groups. So there is demonstrated improvement ?? terms of life in animal studies. So that information is fed through federal government and says that this drug looks promising therefore lets start testing it in humans. The first part of that testing process goes through a ?? base process where the first two phases are to look to see how the drug is handled by the ??? ?? and then once it has been shown you know how the drug gets eliminated from the body and those sorts of issues the next question is, is it safe at increasing doses. Safe in terms of does it cause damage to the lungs, ??? and those tests have been done in humans and the drug is shown to be safe. Now the last phase for federal FDA approval ??? shown in those

patients. Its efficacy has been shown to be basically reducing the amount of blood that was necessary in heart patients undergoing heart bypass surgery. It has not been tested in the population of trauma patients to look to see if it would improve their outcome. That is the study that we are about to undertake. I think that it is going to be beneficial because it does the things during that "Golden Hour" that we need to accomplish and that is to improve blood supply by carrying the oxygen to vital organs so that we have a fighting chance. Could it cause problems? Sure it could as it increases the blood pressure which this medicine does very shortly after giving it the blood pressure goes up so as the blood pressure goes up we may find that the bleeding increases that has not been shown in the case in animals studies but it might be in the human study that is why ?? those results in animals may not be the same in humans.

Question: ???

Thom: High blood pressure, no, there is a couple others that are fairly common ?? one is that ?? discolor the skin in transient meaning that the medicine that lives in the skin for a period of up till five days and ????? eliminate through the body and as such tends to turn the skin a yellow color. You might appear to be jaundice ?? Jaundice will leave you ??? medical doctors ?? usually means that there is a problem with the liver and the patients that have gotten this medication and there skin has turned yellow there liver can actually ???. What has been found is that the medicine

itself is in your skin and with a light shining on it it turns yellow like babies that have high bilirubin levels shortly after their born. It is the same sort of thing. The other common side effect is ????? and some of it ????. Now other side effects that I do not think we will see in our population because our patients are so sick they won't be able to complain. Often times ????
but bloating, gas pains, ???. Again, I don't think that ????
Now the blood pressure effect can be conceived as an adverse side effect ??? where our patients come in with low blood pressure ???? ?????????? blood pressure can rise up to about 35% where it started from. So if someone starts off low and then goes up to normal ????

Question: ??

Thom: Well again that is the possibility if you start off with ???
It is an enhancement. It is just a substitute for blood ???????

Tape is too low to hear!!

Attachment 19

Community Meeting
Pickett Middle School
Thursday, April 17, 1997

Question (female): You said that you use a blood supply from the red cross which is normally discarded after 42 days because if you use that blood after the 42 days there will be adverse affects. So they take it and with a few modifications now it becomes a blood substitute. Do we know if any if there is any adverse effects from the blood substitute? I mean has this been done before? Do we have results somewhere that say this actually helps or doesn't help or have some side effects?

Answer (TAS): Yes. The way this medication, any medication gets approved by the Food and Drug Administration is a very regimented step wise process. First of all, the medication, our blood substitute in this case, is tested in laboratory animals because they want to see if the drug has potential beneficial effects. In study animals this medication in fact does have a better outcome in animals that were bleed to the point where their blood pressure was quite low. They compared this blood substitute to blood and to other standard ways of trying to increase the blood pressure; salt water solutions, albumin, those sorts of things. The animals that received the blood substitute did significantly better than the animals that received the other treatments. So in laboratory animals, there is no doubt that this medication, this blood substitute has benefit at improving survival from bleeding. Now what the FDA then had to see was, is this medicine, this blood substitute, safe? In other words, if you give it to people will they have problems.

some gas pains after you administer the medicine that are transient. But our patient population will be so sick from their bleeding, they will have a breathing tube in place, be under anesthesia, most likely they won't have these complaints or those problems. So those are the adverse affects that are seen.

Question (same female): Since patients normally have high blood pressure or kidney problems will they be candidates for this? How would you not know that?

Answer (TAS): Well, no we don't know that. The only thing we'll know about these patients most of the time is that they've been injured and when they come to us they have a low blood pressure and evidence of bleeding and, in fact, the person that comes that has high blood pressure under normal circumstances that now presents with a very low blood pressure are at even higher risk of having a bad outcome because their organs, like their kidney, needs to see a higher blood pressure to function. Their organs have become used to seeing a higher blood pressure. So it is crucial especially in those people to get the blood pressure up as fast as you can.

VC: In those situations where people come in as trauma victims preexisting diseases, be it high blood pressure, diabetes, or whatever, all of that takes a back seat to the immediate needs of trauma patients, so we're not worried about treating somebody's high blood pressure. At that point in time your priority is trying to provide cellular nutrients, primarily oxygen, by getting

as much material that carries those products into the body faster than it is coming out of the body.

Question (female): Can you tell us how long this research study on this medicine, I'm calling it now, has been and if we can find out what other ingredients are in this medicine. I mean we first started talking about a blood substitute and now we are calling it an actual medicine. So I want to know some substance other than, you know the hemoglobin being re-oxygenated is what I thought I heard but, I mean medicines are made up of more stuff.

Answer (VC): We sometimes interchangeably call it a blood substitute or a medicine and its because its a little bit of both. What it actually is what Dr. Santora already said. Everyone's blood has hemoglobin. Hemoglobin is one part of the red blood cell but it is the prime part that is responsible for carrying the oxygen to the tissue. Every time you breath in oxygen gets into the lungs and into the blood system then the red blood cells carry it to the different tissues attached to hemoglobin. So what they've done is stripped away the red blood cell and taken the hemoglobin, packaged it so that we can get hemoglobin alone without the other components of blood; what it does is it essentially just buys us time. It doesn't eliminate the fact that we still use blood in conjunction with all the other things. We haven't made that clear, and I want to make that clear, this is just another tool in what we'll be using in trying to save someone's live during the resuscitation process. We will still give blood. You will still get red blood cells, and platelets, and fresh frozen plasma, and saline salt water, and putting in a breathing tube, and

getting you to the operating room. Everything continues, in the same manner. The only thing that we plan to do differently in the study is that when you come into the emergency center and you fit the criteria meaning, your blood pressure is lower than 90, your pulse rate is higher than 120, or your heart rate is in what we call a preterminal rhythm, that it appears that if we don't correct things soon the heart is going to stop functioning properly, then you will be selected to either receive the blood substitute or receive saline. Over time we'll look to see if there is a difference in the two groups of people. If the people that got the blood substitute do better than the people that got the saline. But the substance itself is a blood substitute, not a drug. It's not so important what we call it as long as we understand what it is.

Question (female): I understand it is not important what we call it, I'm interested in what it is. What is in it. What is made of. That's my interest.

Answer (TAS): Yes. It's just hemoglobin. That's all it is.

Response (same female): Do you have any written material that we can have.

Answer (TAS): Sure we do. This blood substitute has been studied for 10 years. Okay? It has been used in patients over the last four years and again it's been going through that step wise process of being evaluated. The way drugs are studied is again, you try to make certain that the drug is safe. Okay? This is one of the first trials to see if this medicine or blood

substitute has made an improvement in outcome. We have demonstrated it has been used in over 350 people to show that it is safe.

Response (same female): Do you know where that was done at?

Answer (TAS): It has been all over - in Chicago, in Boston, in Hartfield.

Question: If this drug has already been given to patients then why do you need to do this study, and how many of those people are now dead?

Answer (TAS): All of them are still alive. The study drug, in this case is a blood substitute, still needs more investigation. The phase that all medicines go through to be approved by the food and drug administration is that they go through this phase to figure our if they are safe first. Okay? And then they go through another phase to see if they have a beneficial outcome difference. In other words if I give, God forbid, you this medicine and I don't give it to the gentleman sitting across the hall and you have the same degree of injury in bleeding will you have a better chance of living than will he? When everything else is equal, in other words, we are going to do the same operations, the same amount of fluid and blood and everything else that we normally do today, the only difference is that we are going to give some people shortly after they arrive to the hospital a small volume of this blood substitute in addition to all of their standard treatment and the other group is going to get an equal volume of salt water and all the

standard stuff that we do.

Question: How will you know if the blood substitute is causing problems?

Answer (TAS): Part of the care that we provide to people after injuries includes tests or various laboratory studies that allow us to look at the damage to liver or damage to muscle or damage to the kidney and that's part of the process of caring for the patient, and in particular when you have a research trial. We want to make certain that there is not any adverse reactions in this population of patients, so we will be looking at those things. One of the things that the federal government wants us to do, if we are going to use this exception to informed consent, is to report to a special panel, a safety panel of people that are not involved with the study at all that are going to see the data, the results of the study as people go through the study and if they find that there is an unexpected high adverse affect rate they're going to shut the study down because they don't want to take that chance that we might have an unexpected outcome that could be negative in this patient population. On the same token, when we forward that information to the safety board if it is overwhelmingly positive, then they will stop the study and say you don't need to look and deprive half of the study population of not getting this medicine, because the people that have received it so far have done so much better than the people that haven't is that this drug is obviously good under these circumstances and then the FDA will say we approve this drug, use it on everybody in this circumstance.

Question (male): Who do you expect will be the main people involved in this study?

Answer (TAS): It's to help anybody who comes into our emergency room that has low blood pressure from bleeding. It doesn't matter what race, creed, or age.

Response: Well I've been to MCP's ER and I saw black patients not getting the same treatment as other patients.

Answer (TAS): Well I'm telling you that, I'm standing here today and I will refute that with you as long as you want to have that refuted.

V.C.: I support what Dr. Santora says, but I think we are getting away from the main issue.

Response: Well I think how we're treated is the issue.

V.C. - Let me say this is one of the reasons that I have a personal interest in this study. Do you know what the number one cause of death in young black men between the ages of 18 and 35 is.

Response: Yes, trauma. Now let me ask you who else is in this study?

V.C. - This trial includes 35 centers across the county. Some of the hospitals that have already started the trial are Allentown Hospital, Washington Hospital. Hospitals that are inner city as well as hospitals that are in the suburbs.

Question: Do you have data in writing

V.C. - Everything that we are saying here is documented in prior research articles. Everything we're saying here is documented.

Response: How come we haven't heard about any of the other studies?

TAS - The allentown study has been in the Inquirer. It was in the Inquirer about a month ago.

Question: Could I go to your hospital and get any of this information. I would really like to have it so I can read it before the study starts.

TAS - Sure. We have some background information.

Question (female): I was surprised that you didn't bring something for people to see. You are taking community opinion about this. How and when will you determine what the community decided. From this group of folks here tonight? What?

Answer (TAS): You are a representative of our community.

Question (same female): Is this a one time shot presentation?

Answer (TAS): We have made ourselves available to the community that we serve. This area is only one part. There has been three separate meetings that we discussed this research trial at and we have had a radio show. We have had a newspaper article and the issue of reaching out to the community, I will tell you is a new phenomenon. Okay?

Question (female): So how when will you make your determination yes or no? I need to know that. Without anything I can look at in terms of these 350 people, sure they may be alive but what is the quality of their life. People want to live, but they want to have a good quality of life. So for me, I need to know that because there is a lot of things vivid in my mind regarding African Americans and medical care and research and all of that and it has not been our favor. Frankly, I feel. I need to see something. For me to sit hear and listen to you tonight and say oh this wonderful to save people's lives I wouldn't want that for my family or anyone else's family in this community that I work in and serve in and live in.

Question (female): Now you say this is a blood substitute?

Answer (TAS): This is a blood substitute. Yes.

Question (female): From what I understand the reason why you are out here is to get our response. So if somebody comes into the hospital as a trauma and then gets it will be because of our approval?

Answer (TAS): That is somewhat what we want to do. We certainly want the increased awareness. This is a multi-fold process. We are out here. If we heard absolutely negative things from you saying we wouldn't want to be involved in any kind of research I don't care what if, ands, or butts about it, we wouldn't want to be involved. We would take that back and we would discuss that, but the important issue if nothing else happens is the education that is going to occur tonight. I don't know how many of you have thought about just how grave this problem is for our community.

Question (female): From what I understand this particular medicine ??? is not going to do ?? so

Can't hear.

Question: One you said something about they wanted to test it on people to see whether or not there is any adverse affect, I thought the procedure was to do research on animals to see what side effects then if there weren't then you'd test it on people.

TAS: That's been done.

VC: Animals trials have already been done as well.

Question: Isn't this a trial area here.

VC: This is just a different patient population. Human trials already been done on stroke victims, and patients undergoing cardiac bypass surgery. This is now trials on people who are severely traumatized with bleeding injuries.

Question: So that 350 is that the total number of people in the research or was that 350 out of another number.

VC: That's 350 people that have already received the blood substitute. This trial that were undergoing will hopefully comprise a total of 850 across the 35 centers in the country that are participating in evaluating this substitute on trauma victims, so this is a different patient population.

Question: How long are you going to follow these 350 people? How long are you going to follow them to see if there are any side effects.

Answer (TAS): The blood substitute lasts in the body about 48 hours. Okay, the various trials have looked at them for months but once the medicine is out of the body it doesn't have any

lasting effects. All the effects of this blood substitute are transient in nature. In other words, they come very rapidly and then they go away as the medication is eliminated from the body.

Question: You mentioned something about the panel. The panel is only going to be made up of medical professionals or are you going to allow the community to partake on the board.

Answer (TAS): Well there is actually a number of panels and Ms. Denega and Ms. Schieffield sit on our what we call the Committee for the Protection of Human Subjects. Any hospital that does research has to have a panel of people that are comprised of investigators, legal people, representatives from the community that will review each and every study protocol. In other words, the investigator, our plan to look at this study medicine has been reviewed by this panel of people at our hospital. In addition, this plan has been reviewed by the federal government and both of those panels in every one of the 35 centers that will enroll patients in this trials will have a similar panel at their hospital and will have to review the plans and demonstrate to themselves that this medicine or blood substitute is more safe than it is risky and more importantly, that it has the potential to be beneficial to the people in this circumstance.

Question: What country are the patients from that already received the blood substitute?

Answer (TAS): United States

Question: Does the hospital purchase the drug or does the drug company donate it.

Answer (TAS): The drug company provides the blood substitute.

Question: So they are giving you the drug?

Answer (TAS): That's right.

Question: What drug company is that?

Answer (TAS): Baxter Healthcare

Question: I just have a question - this will only be used in the trauma center? Correct? Someone going there for routine surgery that might need blood on hand during surgery will not have to decide on this substitute.

Answer (TAS): At this point, No. Only people who come in severely injured.

Question: Okay, now who decides who gets it and who doesn't? I mean if your researching you need something to compare it to. All things being equal if two people come in with multiple trauma or whatever, somebody gets saline and somebody gets the blood substitute - who makes

that call?

Answer (TAS): There will be a box or a shelf that will have a series of sequentially numbered envelopes and as soon as the patient comes in an they have injury with low blood pressure and evidence of bleeding then that patient regardless of their color, regardless of their gender, regardless of their age, will be enrolled in this trial. And what that enrollment will entail is that the individual will go to that drawer and pull out the next envelope what ever is on that selection will be the choice made for that patient.

Question: When they come in they may be coherent, but they may not been to one of these neighborhood meetings, but they don't know they are getting a substitute. When you say you need blood they may give their consent without necessarily knowing that they're getting a blood substitute. So even you know with the exception to informed consent and informed consent to be very close and even if someone comes in knowledgeable about this and want this and they get an envelop that says saline. They have to get saline?

Answer (TAS): That's correct.

Question: How do you spell your name?

Answer (TAS): S.A.N.T.O.R.A.

Question: Out of all the people that has been exposed to this study so far do you know the racial breakdown?

Answer (TAS): No I don't.

Question: At all?

Answer (TAS): No

Question: And you said that this information in terms of the study is available? Can you tell me how I can obtain that information?

Answer (TAS): The study that we are proposing to you today? I can send it to you.

Question: What hospital do you work for?

Answer (TAS): Allegheny, MCP.

Question: We need to see things. For me, I need to see things and I know a lot of these people here, members of the team, and we need to see things because if you are going to treat someone who is unconscious based on our decisions whether you want to go with this or not, well, that's

a responsibility. My other interest is this drug company who is making this drug and giving it to you, why? What is their interest?

Answer (TAS): The interest is obviously companies want to develop medicines that ultimately if they prove beneficial they can make money from. I mean that's reality.

VC: This study isn't any much different than every drug that has been developed - that goes to developmental trials. Where it goes to different phases of research until that drug proves itself to be beneficial regarding health care.

Response (female): But they never come into the community and say do you want this or not?

VC: No. It is because this particular protocol has the stipulation of community disclosure and that is why we are here. The point is if the FDA did not say that with this protocol you need community disclosure then we would be doing it the way most research is done. That is you come to the hospital and you are asked if you would like to participate in a trial called this particular drug. Sometimes trials are done in fact, one gentlemen asked about what country. In fact, some drug companies, because it is easier to do human studies over seas in countries that have less stringent regulations. But at the same time, when people find out about some drugs that are being used in other countries and not being used here, people may get upset because that drug is not available. There are complaints that the FDA drags its feet and takes

too long to approve a drug and people may be dying from lack of receiving this drug. So the FDA sometimes gets stuck between a rock and a hard place. Sometimes they say we too slow with approving drugs and then sometime people say well it needs more research and we should take longer to study. What we are trying to say is - we're not trying to say that this drug is on the level of penicillin or anything that is going to revolutionize medicine, every victim that come in the hospital resulting from trauma life is going to be saved, that focus is not here. What we expect and what we hope to project is that we may be able to improve our care to these people. 40% of people who come in with sever trauma die. We hope to try to decrease from 40% to 30%, which means a 25% decrease in the amount of people that die. And again, this is just one more tool at an attempt to try and save people's lives. Again we don't propose this is going to be again a miracle drug. This is just one attempt to try and identify if in fact this drug will be helpful. We came here very expectant that there would be a lot of sensitivity to issues that this protocol is going to be something that maybe tested on blacks or indigent population alone, people who don't have as much of a voice to say aye or nay. This protocol is not concentrated on inner-city or suburbs and it is hopefully evenly distributed.

Doreen D: I think the important thing to do is to let you know that this type of research would not be done. The government thought that this type of research was so important that they created an exception. This is a just a new exception to the law that would allow researchers to come into the community, talk with the community and say will you give exception to the informed consent so we can try this important research. Again, nothing with age, sex, women have been told that they been discriminated against in research. It has nothing to do with it.

The government thought that the trauma research was so important that they wanted to carry out trauma research so that they would create an exception to the law.

Question: What I can see. Let me ask you this. How long ago has it been the 350 people in the study. Has been it long enough to see any long term side effects? Has it been a year? Two years? A month?

Answer (TAS): It has been over the last four years that those people have been

Question: Were they all given it at one time or a few over the four years?

Answer (TAS): past the four years.

Question (can't hear):

Answer (TAS): I think what I am hearing is a lot of skepticism and we expected that and you have every right to be skeptical. But I'll tell you if we or others that follow us can't do these types of research because people have skepticism because of track records.

Response: You don't think that we have reason to be skeptic?

TAS - Absolutely. There is no doubt about that. But the reality of life and we know this is that people in our community are dying left and right.

Response: I understand that.

TAS: And if the skepticism that you have will keep you from having an open mind about potentially beneficial therapies then unfortunately that's how it's going to be cause we're not going to have the tools to be able to change the outcome.

Response: But see I don't want to be one who you come back to latter on after 300 or 400 people have come up with something with really weird or their children have birth defects and say you are people in the community that wanted this. It just strikes me really odd, and this is my own personal opinion that the decision lies with the community - you know that's my own feelings about it and I need to express that. Yeah because I don't want to have that responsibility, whether its my child or not. For someone who couldn't make that decision on their own for us to say, you know, for me to say it's fine go ahead and do it and then later on, you know, their kids are messed up or whatever. I wouldn't want that, that's why people want to live, but people want to live with a good quality of life and until I see something from someone who has had this.

Answer (TAS): How would they ever get that Ma'am?

Response: I don't know, but that would be ridiculous for me not being knowledgeable of this and say yeah.

V.C.: That probably isn't - you know I don't know how realistic that is. A person that comes in trauma may have a hundred things done to them. That person can't say because of the blood substitute I am now this or I am now that. What you do is you try as best you can to identify if there is a significant indicator that says that people have similar injuries yet this one appeared to do better overall then this person.

Response: Well, you give blood to patients that are approved by the FDA that come in and have to have an operation or something and they're in a trauma - you treat them. You treat them anyway. You give them so many cc's of this and that - these are things that are already approved by the FDA and you use those tools and you treat the patient. Why is it now that you can't do the same thing.

Answer (TAS): Despite that 40% of people die.

V.C.: Stop here. Just because you save some people. You say oh well, we're saving 60% of people so we don't need to do anything further?

Response: That's not what I am saying. You treat people now with drugs that you didn't get

the community's say. It's approved by the FDA and you treat people with these drugs, why not use the same procedure with this.

Answer (TAS): Because as a community you need to know what we're doing.

Response: Yeah, we agree with that.

Question: right of a patient. At that point you don't have any rights.

V.C.: You haven't given up your rights.

Response: It is to me, and I'm afraid to do that. It's just a door that is opening because if the federal government is saying now that you can introduce a drug and you don't have to get the patient's consent to use it, that is giving up the patient's rights. Just because of his condition and what ever else is going on. You know, once you start this you will open this pandora's box. How far is this going to go. What's going to come up next year. Well, we can do education if the doctor feels it is necessary. To me, that worries me, with the clinical studies being able to just do it without patient's permission.

Answer (TAS): You have every right to be skeptical about that first off. The issue really revolves around how big you perceive the problem that are faced by this particular patients.

These people are dying. Okay? And we are able to save 60% of them and that sounds like a big number and in fact it's not bad, but you something we have been able to do that for 50 years. We haven't been able to

Question: This isn't the cure all either, I don't believe.

Answer (TAS): And we don't think so either. There are people that come into our hospital and despite anything they need a miracle and this is not a miracle, but we need to have better tools, there is no doubt about that and the issue is that the only way that we can test tools is to be able to do them in the people that are fighting for their lives and under those set of circumstances, the patient is always going to have this quandary of you know, are they really able to understand what we are talking about to give informed consent, because it is tough to do informed consent.

Question: But there are patients with like blood disease, like leukemia.

Answer (TAS): Yes Ma'am. There is no doubt about that.

Question: Why are there not any clinical studies on those patients.

Answer (TAS): That's not what we are asking of this medication. We know that the drug carries oxygen. We know those things.

Question: Those things will benefit those patients as well?

TAS: What do you mean? What things?

Response: The blood drop. The blood levels drop and they need the oxygen supply to their organs as well. If that blood works with the trauma patient would it also work with the patient that had leukemia.

V.C.: Those are different, very different diseases. People who have leukemia have problems with the production of white cells by cancer tissue. That and oxygen supply are two different things. Again, I just wanted to clarify that. The blood does many things. The blood carries oxygen, carries nutrients, carries proteins, it carriers clotting factors. This is just one part of what blood does, carry oxygen.

Question: I am speaking from personal experience. My sister is a patient at Marriah Farm Hospital in North Carolina. Her first amputation wasn't very successful. The second amputation she did receive blood substitution. I don't believe that she is not living today because of the blood substitution, however, she did survive six months after blood substitute. My family however, does not feel that way. They feel very negatively about the blood substitute.

V.C.: I doubt it was this blood substitute.

Question: Well how many are there?

V.C.: When you say blood substitute. There may be many things that lay people may refer to as a blood substitute that may not necessarily be.

Response: I'm quoting exactly what the nurse said to me when I called the hospital to see how my sister was doing.

Answer (TAS): Was your sister a Jehovah Witness.

Response: No, no she's not.

TAS: The reason that I say that is that Jehovah Witnesses have a religious reasons, but they will take a blood substitute, but not this blood substitute because this particular blood substitute is made from blood cells. I'm just trying to clarify this. Again, this must be very frustrating to you because this is complicated stuff and some of the things that we say may seem that it is conflicting because

Question: Does this drug have a name?

TAS: Yes. This stuff is called, Diaspirin Cross-Linked Hemoglobin.

Question: Spell it please.

Answer (TAS): The commercial name is hematest. H.E.M.A.T.E.S.T. Diaspirin Cross-Linked Hemoglobin. D.I.A.S.P.I.R.I.N. Cross-Linked H.E.M.O.G.L.O.B.I.N. So what we are before you today is to talk about the blood substitute that is made from human red blood cells that has human hemoglobin and the process of making this blood substitute is called Cross-Linking and what happens is this blood is obtained from the blood bank because it sat on a shelf longer than 42 days. The drug company prepares this by breaking the coating of the red cell and then cross-linking the hemoglobin so that it can carry oxygen.

Question: Cross-linking it with oxygen?

Answer (TAS): Cross-linking so that it stays together. Hemoglobin is made of four parts and it cross links the two strands so that they stay together.

Question: So you use something to cross-link it?

Answer (TAS): Diaspirin.

Response: Okay, that's why I was asking what was in it. I knew it wasn't just hemoglobin.

Answer (TAS): But it's all hemoglobin. But the important thing - this is very important. When the drug company makes this it takes the blood that's been screened for HIV and all the viruses in the process of donation through the red cross, it takes those precautions and to that it adds heating this hemoglobin and filtering it and pasteurizing it which makes this product much more unlikely to transmit viruses which are inactivated by heating and pasteurization. So in essence, this blood substitute has less change of transmitting AIDS or any other virus than blood banked blood.

Question (male): I'm saying that all the research and studies you know no racial breakdown at all?

Answer (TAS): I have to say that I don't know. I really don't know. I don't know the breakdown.

Question: But you can get that breakdown right?

Answer (TAS): I don't know.

Question: Do you have any other plans for community meetings like this? And will you have

a scheduled time line for implementation?

Answer (TAS): We would like to see this be the last meting that we have. We've had two other meetings in area communities and pardon me.

Question: Where were the other meetings?

Answer: At Deveraux Church in North Philadelphia and in East Falls.

Question: How will we find out the results of the study?

Answer (TAS): The thing that we can do is to send a letter to each of you who sign into these meetings and to key individuals that we've identified in the community to tell them about these meetings at the completion of the study we will tell you when we will have a meeting to discuss the outcome of the study. That's what we owe to the community.

Question: Can we ask if it was favorable or non-favorable at those other two community meetings?

Question: It was not during the amputation that the blood substitute was given. She wa four days post-operation and was given this. She had very low blood pressure and she was dying and

this is when they gave her the blood substitute. I just wanted to clear that it was not given to her in the appearing room during surgery.

Answer (TAS): Was that as part of the research program, Ma'am.

Response: I did not find out about the blood substitute until I called to check on my sister and I was told at that time that they almost lost her and they had to give her a blood substitute and that was what concerned me. I was basically the contact person and I don't recall anyone trying to reach me.

V.C.: Under those circumstances, if it was this, if a person they can identify as someone who can give consent, they would not do anything. They would not enroll anyone who has the ability to give consent without obtaining that permission. The only time with this study that we would do that is if there was no one available. If there is a contact, someone was in the emergency room, if there was a name on the chart or anything identifying as someone who can give consent, that person would absolutely have to be notified and their consent would have to be given.

Response: I am going to request the hospital report. Because I know for a fact it was told to me that it was a blood substitute and they did have a contact person.

Answer (TAS): We don't even know if that situation was the same blood substitute.

Response: I did also mention that it may not have been the same blood substitute. How many are there?

Question: How many are you using?

Answer (TAS): There has been a number of blood substitutes that have tried to be developed because the blood bank business realizes that there is a lot of blood that sits on the shelf that doesn't get uses. Because with blood you can only give blood to someone who has the exact blood match to your type of blood and these blood substitutes, one of the beneficial aspects of these blood substitutes is by stripping off the coating that has all of the markings for their blood type you can give this hemoglobin to anyone. You don't have to give a blood type. So that's one of the advantages of this blood substitute.

Answer (TAS):

Answer: That's

Tape ended.

Attachment 20

000-000145

Margeret M. McGoldrick
President and Chief Executive Officer

ALLEGHENY
UNIVERSITY
HOSPITALS

Allegheny University MCP
3300 Henry Avenue
Philadelphia, PA 19129
215-842-7167
215-843-4074 Fax

Allegheny University I Bucks County
225 Newtown Road
Warminster, PA 18974
215-441-6601
215-441-5677 Fax

Allegheny University H Elkins Park
60 E. Township Line Roa
Elkins Park, PA 19027
215-663-6366
215-663-6033 Fax

April 1997

Dear Key Community Member:

Allegheny University Hospitals, MCP has been chosen to participate in a research study for a new blood substitute for trauma patients. This research could potentially prevent the harmful effects of blood loss in severely injured patients. Because of the unique aspects of this research, we are hosting community meetings to discuss this research and its impact on the community.

When researching new medical treatments, the first step is ensuring patients understand the study and voluntarily consent to participate. However, emergency medical situations where life and/or limb is in jeopardy present a unique challenge. Due to the severity of the injuries, it is usually not possible to obtain informed consent from a trauma patient or an immediate family member before the patient requires treatment. Thus, it is difficult to develop new and better therapies for trauma care. For that reason, this study is to be performed with an "exception to informed consent," meaning that in most cases written approval will not be obtained from the patient prior to treatment.

These meetings are being held to inform and gain feedback from the community about this potentially life-saving treatment. You are invited to join Drs. Thomas Santora and Vincent Cowell, the Allegheny MCP physicians conducting the research study, who will:

- explain the nature of the study;
- outline the risks and benefits of the study;
- discuss the concept of exception to informed consent;
- present patient and community safeguards; and
- answer questions.

The meetings have been scheduled for:

Friday, April 11, at 7 p.m.	Wednesday, April 16, at 7 p.m.	Thursday, April 17, at 7 p.m.
Devereaux United Methodist Church	Falls of Schuylkill Library	C.E. Pickett Middle School
26th & Allegheny Avenue	Warden Drive & Midvale Avenue	Wayne & Chelten Avenue

I hope you (or one of your representatives) can attend one of these meetings and give your valuable input. Research concerning severely injured trauma patients could one day save your life or the life of someone you love.

For more information, please call 1-800-PRO-HEALTH℠.

Sincerely,

Meg McGoldrick

Meg McGoldrick
President and CEO, Allegheny University Hospitals, MCP

Attachment 21

Published in The
Valley Item
April 17, 1997

Also in:
"King of Prussia Post"
April 10, 1997

Similar article in "The Falcon" 4/18/97

New blood substitute could save more lives

By C.L. Chase
Staff Writer

Everybody is at risk, one time or another, of losing copious amounts of blood in vehicle crashes, shotgun wounds, stabbings and falls from heights, among other accidents.

Approximately 140,000 Americans die annually because of bleeding from accidents, according to Dr. Thomas Santora of Allegheny University Hospital, formerly the Medical College of Pennsylvania, in Philadelphia.

Santora said in an interview that a new blood substitute, HemaTest, will undergo evaluation through research that he and a colleague, Dr. Vincent D. Cowell, are spearheading at the hospital, scheduled to begin May 1. He added that 35 hospitals around the country are also planning to engage in this research.

One of their goals, Santora said, is to help reduce the annual mortality rate, because of bleeding, by approximately 30,000 people.

Another goal is to determine if combining infusion of large amounts of salt solutions (given intravenously), conventional blood transfusions, and control of bleeding during surgery – all conventional treatments – with HemaTest will enhance results.

An ultimate goal is to use HemaTest in severe accidents in the suburbs or elsewhere when victims are airlifted to trauma centers in Philadelphia. Trauma surgeons and emergency room physicians refer to the "golden hour," Santora said, explaining that doctors have about 60 minutes after arrival of a victim to improve the blood supply and control injury in an injured person. "Time is of the essence," he said.

Santora went on to say that Allegheny is in the "last phase" of the federal Food and Drug Administration approval program. HemaTest, produced by Baxter Healthcare of Illinois, has been used over the last four years on patients in hospitals throughout the country to demonstrate safety. Results were good, he said. Other Philadelphia hospitals are in the planning stage and, according to Santora, chemical compound known as Flousol was developed and used for a number of years. It consisted of a protein similar to hemoglobin – Santora described it as a fluorocarbon – that carried oxygen into the bloodstream.

The new medication is actual hemoglobin, Santora said, that has been extracted from donated blood that has been screened for viral contamination. Donated blood, even if kept refrigerated, has a shelf life of 42 days. "After that," he said, "it is no longer usable as a blood transfusion product."

Santora said that people who qualify for the study must be older than 18; not pregnant if female; or with low blood pressure.

He emphasized that his work, and that of his colleague, Dr. Cowell, are in a research stage. "We're trying to educate the public about the seriousness of severely injured people. The product has shown to be safe. Now we have to show its effectiveness."

Santora also stressed that use of this new medication would, insofar as possible, be used on "informed consent" by the patient. If the patient is unable to give such consent because of his or her condition, a relative may be brought into the picture, if that is possible.

If all else fails, he said the federal government has made provision for investigators to provide treatment in life-threatening situations without informed consent.

Four-year studies in other hospitals have shown three types of adverse reactions, Santora said. They include an above-normal increase in blood pressure; the skin may show a yellow discoloration, which he said is temporary and goes away within five days, and does not affect the liver; and a patient's urine can temporarily turn red but usually clears up in about 48 hours. Other less common side-effects are an elevation of an enzyme in the pancreas, a transient occurrence that lasts for two to five days; and abdominal gas pains, also transient, that last for two to five days.

Anyone interested in this research program can obtain

Attachment 22

...Page 10 | East Of Germantown Ave., 6/16- 6/20 | See Calendar, Pages 14, 15, 17

Germantown Courier 47

Serving the Germantown community since 1936

Questions, distrust at forum on blood substitute

By JUDY HARTHEIMER
Correspondent

Doctors Thomas Santora and Vincent Cowell, both physicians at Allegheny Medical Center East Falls, came to a Germantown community meeting last Thursday to explain the hospital's participation in a drug approval study.

They were greeted with plenty of hard questions and distrust from the audience last Thursday evening at Pickett Middle School. The meeting was chaired by local activist Supreme Dow, head of the Northwest Leadership Training Academy.

Allegheny East Falls has been approved by the Federal Drug Administration as a testing site for a new blood product called DLCBh (Diaspirin Crosslinked Hemoglobin), which is created from some of the byproducts of expired red blood cells, according to the doctors. The hope, they said, is that DLCBh can be proven effective in helping to save trauma patients who are bleeding so severely that they are in danger of dying.

But most of the approximately 50 area residents who attended the meeting saw it differently. The hospital, they said, was trying to use the mostly African American community it serves as guinea pigs for a product that might not be safe, and the company that produced the new DLCBh stood to make immense profits at the expense of the community.

Compounding the widespread distrust was the fact that the Allegheny study would be the first in the nation to use a change in federal regulations issued last year that allows "exception to informed consent," which means that in life-threatening situations hospitals participating in an approved study can administer experimental drugs to patients who are not capable of giving consent.

The informed consent issue alone was enough to draw fire from community activist Sheila Laney, head of the Block Captains Association of Southwest Germantown. Laney said she was totally opposed to the use of experimental drugs, even in cases where physicians hoped to save lives, on patients who were unable to give their consent. "I have a big concern that you will be giving people experimental products that have not been tested," said Laney.

The new regulations were issued by the U.S. Food and Drug Administration in September of last year. The FDA release outlining change said, "The exception would apply to a limited class of research activities involving human subjects who are in need of emergency medical intervention, but who cannot give informed consent because of their life-threatening medical condition. The FDA is taking this action in response to growing concerns that current rules are making high-quality acute care research difficult or impossible to carry out at a time when the need for such research is increasingly recognized."

Laney and many others at the meeting also questioned the proven safety of the new blood product. "Exactly how many trauma patients have been given this product for you to say that it's safe?" she asked the doctors.

They replied that DLCBh had been tested for ten years on animal subjects, and for the past four years on humans. The study at Allegheny East Falls will be replicated at other hospitals across the country, and is the last step before FDA approval to market the blood product. The compound helps trauma victims, said the doctors, because it is a carrier of oxygen, and can help sustain the function of vital body organs that are in danger of failing because of massive blood loss.

Under the rules of the study, they said, all patients would be given the current standard treatment, and some would be given the DLCBh in addition.

The doctors acknowledged that many subjects in the study might very well be members of the community around the hospital, including victims of violence. "Until we get violence under control we are going to see people come into our trauma center and die in spite of our best interest," said Santora. "Primarily, young people are dying because the technology isn't good enough."

The doctors' statements of good intentions weren't enough to quell the distrust of audience members who said the African American community had been victimized too often by institutions that claimed to have its best interests at heart.

"It seems that the black community doesn't trust any studies," said audience member Vincent Muhammad. "We need to develop our own means of investigating," he said. He also questioned whether figures on the racial background of the people used in the study would be available.

Others in the audience questioned the way the hospital approached the community. "Why didn't you come to the community before you applied for the study?" asked Gerald Calliman, representing Concerned Neighbors of Greater Germantown.

There is no firm date for the start of the study, although it has received clearance from the FDA. Santora said that enough direct opposition from the community could block the hospital's participation.

Attachment 23

INNERVIEW

ALLEGHENY UNIVERSITY HOSPITALS
MCP

Allegheny University Hospitals Begins Development on Program for Digestive Health

To improve patients' digestive health through education and to make cutting-edge technological advances in surgery and medicine readily available to patients who suffer from diseases of the digestive system, Allegheny University Hospitals is currently developing a new Program for Digestive Health.

The Program will enhance current therapeutic and diagnostic endoscopic procedures used for diagnosing diseases of the digestive system, and build upon established strengths within the hospital system in the areas of partial hepatic resection surgery and colorectal surgery, as well as the evaluation and treatment of patients who suffer from pancreatic diseases, inflammatory bowel disease and gastro-esophageal reflux disease (GERD).

The Program will integrate interdisciplinary efforts in medicine and surgery, with the key goal to deliver digestive health services throughout communities in the Delaware Valley. The efforts in medicine will be headed by James C. Reynolds, M.D., Professor of Medicine and Chief of the Division of Gastroenterology and Hepatology at Allegheny University of the Health Sciences. Joel Roslyn, M.D., Professor and Chair, Department of Surgery, will lead the efforts of surgeons from a number of surgical subspecialties in the Program.

The Program will have several practice locations, including sites at Allegheny University Hospitals, Hahnemann, Allegheny University Hospitals, MCP and St. Christopher's Hospital for Children. Each of the hospital sites will provide leading-edge treatments using advanced surgical and medical technology. Nationally and interna-

continued on page 3

ood Substitute Holds Promise for Trauma Victims with Severe Blood Loss

Every year, more than 140,000 Americans die from injury, many of them from severe blood loss that can result from car accidents, gunshot wounds or other trauma. In fact, of those patients who suffer extensive blood loss, 40 percent die despite state-of-the-art trauma care.

Now, a promising new treatment – a new blood substitute called Diaspirin Cross-linked Hemoglobin (DCLHb) – is about to be made available as part of a research study at Allegheny MCP's Trauma Center. DCLHb potentially could prevent the harmful effects of blood loss in severely injured patients. Simply put, this study could save lives.

When a patient loses a significant amount of blood, blood pressure drops, the body's organs don't receive enough oxygen, and shock can set in. When introduced into the circulatory system, DCLHb counters the effects of shock in two ways – it works to raise blood pressure and to carry oxygen to vital organs. It could reduce the need for blood transfusions, and requires no blood type matching process.

In animal studies, this treatment has improved blood flow to vital organs. Over the last four years, DCLHb has been studied. It has been fully reviewed and cleared by the U.S. Food and Drug Administration (FDA) and has received favorable review by our hospital review board and numerous regulatory agencies around the world.

This new investigative treatment will be made available only to the most severely injured trauma patients, including males or non-pregnant females older than 18 who present in shock conditions despite prehospital treatment, and who have evidence of hemorrhage. Immediately following hospital arrival, emergency medicine physicians will assess the patient for entry criteria. Those

continued on page 4

Blood Substitute Holds Promise for Trauma Victims with Severe Blood Loss

continued from cover

patients meeting the entry criteria will receive 500 - 1000 cc (approximately the volume of two to four soda cans) of DCLHb or equal volumes of salt solution placebo within 60 minutes of arrival in addition to all standard interventions (salt solution, blood transfusion, operation or a combination of all). By the design of the study, the physicians will not know at the time of randomization whether a patient will receive DCLHb or the placebo solution. All patients will be followed closely for 28 days after treatment.

When researching new medical treatments in emergency situations such as this, ensuring that patients understand the study and voluntarily give consent – normally required in any clinical trial – presents a unique challenge. Due to the severity of the injuries, it is usually not possible to obtain informed consent from the injured patient and frequently family members are not immediately available before the patient requires treatment. However, excluding patients who cannot give consent under these life-threatening conditions would make it difficult to develop new and better therapies for trauma care. For this reason, this study is to be performed under the new approved FDA guidelines for the "exception to informed consent," meaning that treatment can still be administered in these cases where it is impossible to obtain written approval. Since the patient cannot give consent at the time of the injury, the FDA guidelines stipulate that the community from which the patients are expected to come will be informed of the proposed research project.

Allegheny MCP is taking steps to make the community at large aware of this study and to answer any questions or concerns. An internal review board is overseeing the patient safeguards and community education programs that address the needs and concerns of the community.

A key part of this public disclosure is a series of community meetings being held to inform the public about the proposed research project and its potential to save lives. All community members and hospital staff are invited to join the Allegheny MCP physicians conducting the research study – Thomas Santora, M.D., Associate Professor of Surgery, Associate Director of The Regional Resource Trauma Center, and Vincent Cowell, M.D., Instructor in Anesthesiology and Trauma Anesthesiologist– who will explain the nature of the study, outline the risks and benefits of the study, discuss the concept of exception to informed consent, present patient and community safeguards that have been put in place, and answer questions.

The meetings have been scheduled for:

- **Friday, April 11, at 7 p.m.,** at Devereaux United Methodist Church, 26th and Allegheny Avenue, Philadelphia
- **Wednesday, April 16, at 7 p.m.,** at Falls of Schuylkill Library, located at Warden Drive and Midvale Avenue, Philadelphia
- **Thursday, April 17, at 7 p.m.,** at C.E. Picket Middle School, located at Wayne and Chelten Avenue, Philadelphia

Faculty, staff, employees and students are welcome to attend these meetings and give valuable input. Research concerning severely injured patients could one day save your life or the life of someone you love. ◆

New Monthly EAP Parenting Support Group Formed

The Employee Assistance Program (EAP) has created a new parenting support group that will meet during lunchtime on a monthly basis. The group will provide support for parents and grandparents who are caring for children of all ages.

Topics will include:

- How to stretch your time with your kids
- Ways to be creative with your kids
- At what age should kids get certain responsibilities
- Areas of interest or concern you may have as a parent
- Basic exchanges of ideas for parents

The first meeting will take place Friday, April 25, from noon to 1 p.m. in the President's Conference Room on the fifth floor of the hospital. Bette Begleiter, mother of three, EAP Manager, will facilitate the discussion. For more information, call 842-4690. ◆

More than 30 employees, including Sylvia Beck, M.D. (left), Ophthalmology, received free dexa screenings as part of the new Osteoporosis Program at Allegheny MCP. Kendra Zuckerman, M.D. (right), Director of the Osteoporosis Program, interpreted results

Allegheny Cardiovascular Institute to Hold Annual Night at the Races

Enjoy a lively evening with friends at the Allegheny Cardiovascular Institute tenth annual Night at the Races Friday, May 2, at Garden State Park, Route 70 and Haddonfield Road, Cherry Hill, N.J.

Tickets for the event are $60 per person and include a deluxe buffet dinner, admission to the park, Phoenix valet parking, Phoenix admission and a racing program. Doors open at 6:30 p.m.; post time is 7:30 p.m. Gentlemen are required to wear jackets.

The Allegheny Cardiovascular Institute is a newly constituted organization to advise, counsel and support the cardiovascular endeavors of Allegheny Health, Education and Research Foundation. The organization is committed to advancing cardiovascular research, education and patient care.

For ticket information, please call Mari-

Attachment 24

Working Through the Public Disclosure Process Mandated by Use of 21 CFR 50.24 (Exception to Informed Consent): Guidelines for Success

Thomas A. Santora, M.D.*, Vincent S. Cowell, M.D., Stanley Z. Trooskin, M.D.* Allegheny University of the Health Sciences-MCP, Department of Surgery, Division of Trauma & Surgical Critical Care, Philadelphia, PA

Introduction In November 1996, the FDA formalized guidelines for emergency care research to be done under an "exception to informed consent". These guidelines (21 CFR 50.24) mandate community awareness of the proposed research, but provide no specific methods by which to accomplish this task. This descriptive report outlines how our Level I Trauma Center established a community educational program for a study utilizing a blood substitute.

Methods A counsel of leaders from the highest volume trauma communities (HVTC) was established to review the research project and assist in development of our public disclosure (PD) program. Hospital personnel were educated through faculty meetings, hospital committees, in-house publication feature articles and flyers. The community was informed of our intent, purpose and issues related to this research project by a talk radio show, radio public service announcements, advertisements and feature articles in local and regional newspapers. Additionally, three interactive education meetings were held in the HVTC. A call-in line was established for community feedback.

Results An excess of 70 manpower hours were required for our PD. All communities acknowledged the gravity of the problem faced by the severely injured patient. Initial skepticism was encountered about the motivation of the institution to involve the community in hospital activities, the safety of the experimental product, the minority population shouldering an unfair proportion (Tuskegee fallout) of the research burden and the loss of individual decision-making liberty. Though universal community acceptance of this research study was not achieved, the educational process diminished the majority of the community's suspicions.

Conclusions Though PD of clinical research is difficult and time-consuming, the results can be rewarding. The investigator(s) must identify the community, open lines of communication and be prepared for skepticism. The PD mandate of 21 CFR 50.24 to increase community awareness was met through extensive honest and forthright information exchange.

Thomas A. Santora, M.D., Assoc. Prof. of Surgery, Allegheny University of the Health Sciences-MCP, Dept. of Surgery, Div. of Trauma & Surg. Crit. Care.
3300 Henry Avenue, Philadelphia, PA 19129 (215) 842-6567

Thomas A. Santora, MD

Contact: Eryn Dobeck
Ruth Ann Dailey
(215) 842-4533

NEW ADVANCEMENTS IN TRAUMA CARE FOR YOUR COMMUNITY

PSA :15

EACH YEAR CLOSE TO 140,000 PEOPLE DIE AS A RESULT OF TRAUMATIC INJURY. IN MANY CASES, BLOOD LOSS IS THE CAUSE OF DEATH. RESEARCH WITH A NEW BLOOD SUBSTITUTE IS BEING CONDUCTED AT ALLEGHENY UNIVERSITY HOSPITALS, MCP. THIS RESEARCH COULD SAVE YOUR LIFE. FOR INFORMATION, CALL 1-800-PRO-HEALTH.

-30-

Attachment 26

05 PSA Radio/TV

11-1-94

000-000152

MR #

Subject:

Send on PR Newswire?

Send to Provider Plan List?

Mailing Date:

Public Service Director
KYW-RADIO
Independance Mall East
Philadelphia, PA 19106

Public Service Director
KYW-TV
Independence Mall East
Philadelphia, PA 19106

NJN Radio
The New Jersey Station
CN 777
Trenton, NJ 08625-0777

Public Service Director
RADIO INFORMATION FOR THE BLIND
919 Walnut Street
Philadelphia, PA 19107

The PSD News Center/ERC-TC
THE PA SCHOOL FOR THE DEAF
100 West School House Lane
Philadelphia, PA 19144

Public Service Director
WBCB
200 Magnolia Drive
Box 1490
Levittown, PA 19054

Public Service Director
WBUX
P.O. Box 2187
Doylestown, PA 18901

Public Service Director
WBYO-FM
P.O. Box 177
Boyertown, PA 19512

Public Service Director
WCAU-TV
City Line Ave./Monument Rd.
Philadelphia, PA 19131

Public Service Director
WCHE
119 Market Street
West Chester, PA 19382

Public Service Director
WCHR-FM
Woodside Road
Yardley, PA 19067

Public Service Director
WCOJ
P.O. Box 1408
Coatesville, PA 19320

Public Service Director
WDAS-AM & FM
WDAS Building
Belmont Avenue & Edgeley Rd.
Philadelphia, PA 19131

Public Service Director
WDRE-FM
P.O. Box 1188, Suite A-104
Benjamin Fox Pavilion
Jenkintown, PA 19046

Public Service Director
WEAZ-FM
Philadelphia Executive Offices
10 Presidential Blvd.
Bala Cynwyd, PA 19004

Public Service Director
WEGX-FM
3 Bala Plaza
Suite 580E
Bala Cynwyd, PA 19004

WEXP, LA SALLE UNIVERSITY
C/o Promotions
P.O. Box 698, 20th & Olney Ave
Phila.,, PA 19141

Public Service Director
WFIL
10 Presidential Blvd.
Bala Cynwyd, PA 19004

Public Service Director
WFLN
8200 Ridge Avenue
Philadelphia, PA 19128

Public Service Director
WFMZ-FM
East Rock Road
Allentown, PA 18103

Public Service Director
WGLS-FM
Glassboro State College
Glassboro, NJ 08028

Public Serv. Dir.
WHAT
KBT Communications
2471 N. 54th Street
Philadelphia, PA 19131
(215) 581-5161

Public Service Director
"HWH
.O. Box 9750
Trenton, NJ 08540

Public Service Director
WHYY-FM
Independence Mall West
150 North 6th Street
Philadelphia, PA 19106

Public Service Director
WHYY-TV
Independence Mall West
Philadelphia, PA 19106

Public Service Director
WIOQ-FM
2 Bala Plaza
Suite 201
Bala Cynwyd, PA 19004

Public Service Director
WIP
441 North Fifth Street
Philadelphia, PA 19123

Public Service Director
WJBR-FM
2617 Elbright Road
Wilmington, DE 19810

Public Service Director
WKDN-FM
2906 Mt. Ephraim Avenue
Camden, NJ 08104

Public Service Director
WMGK-FM
1 Bala Plaza
3rd Floor West
Bala Cynwyd, PA 19004

Public Service Director
WMMR-FM
19th & Walnut Streets
Philadelphia, PA 19103

Public Service Director
WNAP
Box 11
Philadelphia, PA 19128

Public Service Director
WNJS-TV
1573 Parkside Avenue
Trenton, NJ 08638

Public Service Director
WNPV
Snyder Road
Box 1440
Lansdale, PA 19446

Public Service Director
WOGL-AM/FM
City Line Ave./Monument Rd.
Philadelphia, PA 19131

Public Service Director
WPAZ
Maugers Mill Road
Box 638
Pottstown, PA 19464

Public Service Director
WPEN
1 Bala Plaza
3rd Floor West
Bala Cynwyd, PA 19004

Public Service Director
WPHL-TV
5001 Wynnefield Avenue
Philadelphia, PA 19131

Public Service Director
WPST-FM
Box 9750
Trenton, NJ 08607

Public Service Director
WPVI-TV
4100 City Line Avenue
Philadelphia, PA 19131

Public Service Director
WRTI-FM
TEMPLE UNIVERSITY
Annenberg Hall
Philadelphia, PA 19122

Public Service Director
WSSJ
6th & Market Streets
Camden, NJ 08101

Public Service Director
WSTW-FM
2727 Shipley Road
Wilmington, DE 19803

Public Service Director
WTEL
1349 Cheltenham Avenue
Philadelphia, PA 19126

Public Service Director
WTMR
2775 Mt. Ephraim Avenue
Camden, NJ 08104

Public Service Director
WTTM
333 West State Street
Trenton, NJ 08618

Public Service Director
WTXF-TV
4th & Market Streets
Philadelphia, PA 19106

Public Service Director
WUSL-FM
440 Domino Lane
Philadelphia, PA 19128

Public Service Director
WVCH
P.O. Box A
Brookhaven, PA 19015

Public Service Director
WWDB-FM
166 E. Levering Mill Rd.
Bala Cynwyd,, PA 19004

Public Service Director
WXPN-FM
3905 Spruce Street
Philadelphia, PA 19104

Public Service Director
WXTU-FM
23 West City Line Avenue
Bala Cynwyd, PA 19004

Public Service Director
WYSP-FM
1 Bala Plaza
Suite 424
Bala Cynwyd, PA 19004

Jerry Abear
News Director
WYXR-FM
One Bala Plaza
Bala Cynwyd, PA 19004

Public Service Director
WYXR-FM
One Bala Plaza
Bala Cynwyd, PA 19004

Public Service Director
WZZD
117 Ridge Pike
Lafayette Hill, PA 19444

000-000157

06. PSA-Cable TV
11-1-94

NR #
Subject:
Mailing Date:

Public Service Director
ADELPHIA CABLE
P.O. Box 198
1 Apollo Rd.
Plymouth Meeting, PA 19462

Public Service Director
AMERICAN CABLEVISION OF PA
3 Moore Road
Wallingford, PA 19086

Public Service Director
CABLE TV OF CHESTER CO.
Rt. 82 & Monacy Road
Coatesville, PA 19320

Public Service Director
CATV SERVICE COMPANY
46 North Union Street
Lambertville, NJ 08530

Public Service Director
COMCAST CABLEVISION
29 York Road
Willow Grove, PA 19090

Public Service Director
GREATER PHILA. CABLEVISION
1351 South Delaware Avenue
Philadelphia, PA 19147

Public Service Director
HARRON CABLE TELEVISION
First & Ruthland Avenues
Malvern, PA 19355

Public Service Director
HOME-VUE CABLE TV
4143 Swamp Road
Doylestown, PA 18901

Public Service Director
JONES INTERCABLE, INC.
Box 775
Turnersville, NJ 08012

Public Service Director
LOWER BUCKS CABLEVISION
2320 Trenton Road
Levittown, PA 19056

Public Service Director
MAPLE SHADE CABLE TV
60 West Main Street
Maple Shade, NJ 08052

Public Service Director
NYT CABLE-TV
1250 Haddonfield-Berlin Road
Box 5025
Cherry Hill, NJ 08034

Public Service Director
OXFORD VALLEY CABLEVISION
1750 Byberry Road
Bensalem, PA 19020

Public Service Director
PENN STATE CABLE
114 Ridge Road
Sellersville, PA 18960

Public Service Director
SERVICE ELECTRIC CABLE
1045 Hamilton Street
Allentown, PA 18101

Public Service Director
STORER CABLE COMMUNICATION
Box 50
Willingboro, NJ 08046

Public Service Director
STORER COMMUNICATIONS OF
GLOUCESTER COUNTY
304 South Broad Street
Woodbury, NJ 08096

Public Service Director
STORER RIVERFRONT CABLE
1809 Taylors Lane
Cinnaminson, NJ 08077

Public Service Director
SUBURBAN CABLE
237 West Germantown Pike
Norristown, PA 19401
610-239-2100

Public Service Director
SUBURBAN CABLE TV
2319 York Rd.
Jamison, PA 18929

Public Service Director
SUBURBAN CABLE TV COMPANY
114 Ridge Road
Sellersville, PA 18960

Public Service Director
SUBURBAN CABLE TV COMPANY
20 South Main Street
Phoenixville, PA 19460

Public Service Director
SUBURBAN CABLE TV COMPANY
601 Oak Lane
Glenolden, PA 19036

Public Service Director
SUBURBAN CABLE TV COMPANY
503 South Cedar Lane
Upper Darby, PA 19082

Public Service Director
SUBURBAN CABLE TV COMPANY
3 Moore Rd.
Wallingford, PA 19086

Public Service Director
SUBURBAN CABLE TV COMPANY
261 West DeKalb Pike
Suite EG2
King of Prussia, PA 19406

Public Service Director
SUBURBAN CABLE TV COMPANY
1200 High Street
Pottstown, PA 19464

Public Service Director
TCI OF NEW JERSEY
520 Monmouth Street
Gloucester, NJ 08030

Public Service Director
ULTRACOM OF LANSDALE, INC.
668 Bethlehem Pike
Montgomeryville, PA 18936

Attachment 27

MEMORIAL JOINS NATIONAL TRAUMA RESEARCH STUDY

June 12, 1997

Memorial Medical Center, Inc., is one of about 30 sites nationwide chosen to study the effectiveness of a new blood substitute that possibly could save the lives of trauma patients with severe blood loss. The oxygen-carrying hemoglobin solution is part of a new group of blood substitutes having many potential applications and affecting millions of people. Every year, nearly 1.2 million people sustain severe traumatic injuries. More than 150,000 of these people die, making trauma-related injuries the number one cause of death among Americans ages 1 through 45.

Memorial's research study will test the effectiveness and safety of the blood substitute, **Diaspirin Cross Linked Hemoglobin** (DCLHb), in treating patients with serious traumatic hemorrhagic shock (severe blood loss due to serious injury). Nationwide, a total of 850 patients will be enrolled in this clinical trial. The study is expected to last approximately a year and is sponsored by Baxter Healthcare Corporation. Memorial has been chosen to participate due to the presence of research staff, trauma team, nurses, and lab technicians to support this type of research.

Memorial Medical Center would like to make participation in this study available to its patients who suffer from severe traumatic hemorrhagic shock, even when it is not possible to get informed consent from a family member or legal guardian prior to giving the blood substitute. Accordingly, Memorial Medical Center is taking this opportunity to communicate with the community and inform potential patients, guardians, and other appropriate parties of the potential use of this new product.

Between 10 and 20 patients will be enrolled in the study at Memorial. Half will receive the blood substitute and half will receive a saline solution. In addition, current standard treatment, including blood transfusion when appropriate, will be administered to all study participants.

The blood substitute is man-made and derived from human red blood cells which would otherwise be wasted. It has potential applications in situations where large amounts of blood loss can result in a lack of oxygen to vital tissues. Patients can go into shock, which can lead to multiple organ failure several days or weeks after the initial injury. The blood substitute has been shown to carry oxygen to cells and tissues and seems to increase blood flow to vital organs.

Use of the blood substitute as a supplement to blood transfusions also saves critical time in stabilizing a badly hurt patient because it does not have to be typed or cross-matched. The solution has been heated and filtered to reduce the risk of blood-borne infections. The blood substitute has been studied extensively over a four year period in clinical trials involving more than 700 patients. Of the approximately 350 who received the drug, a few temporary side-effects were noted. These included changes in some lab test results, a temporary yellowing of the skin (unrelated to liver damage), temporary reddening of the urine due to the red color of the product, nausea, and back, abdominal and muscle pain. Blood pressure may be elevated following administration.

Because trauma patients are often so severely injured, they may not be able to give consent to participate in the drug trial, and family frequently cannot be located or reached quickly. For this reason, the U.S. Food and Drug Administration and the Office of Protection of Patient Rights allows waiving consent in studies of emergency therapies when the potential benefits outweigh the risks. It is critical in trauma situations that the blood substitute be given within the first hour that the patient is being treated. Once the families are found, they will be informed of the study and can decide on continued participation.

Media inquires should be made to Derek Smith, MMC Corporate Communications, at (912) 350-6874.

Attachment 28

AIKEN COMMUNITY HOSPITAL
ER NURSE MANAGER
P.O. 1117
AIKEN, SC 29802

ALLENDALE CO.HOSPITAL
ER NURSE MANAGER
P.O. BOX 216
FAIRFAX, SC 29827

APPLING GENERAL HOSPITAL
ER NURSE MANAGER
301 E. TOLLISON ST.
BAXLEY, GA 31513

BACON HOSPITAL
ER NURSE MANAGER
P.O. BOX 745
ALMA, GA 31510

BAMBERG CO MEM HOSP.
ER NURSE MANAGER
NORTH & MCGEE STS.
BAMBERG, SC 29003

BARNWELL CO. HODPITAL
ER NURSE MANAGER
P.O. BOX 588
BARNWELL, SC 29812

BEAUFORT MEMORIAL HOSP.
ER NURSE MANAGER
121 RIBAUT RD.
BEAUFORT, SC 29902

BEAUFORT NAVAL HOSPITAL
ER NURSE MANAGER
RIBAUT RD.
BEAUFORT, SC 29902

BERRIEN CO. HOSPITAL
ER NURSE MANAGER
P.O. BOX 665
NASHVILLE, GA 31639

BULLOCH MEM. HOSP.
ER NURSE MANAGER
P.O. BOX 1048
STATESBORO, GA 30458

BURKE COUNTY HOSP.
ER NURSE MANAGER
351 LIBERTY ST.
WAYNESBORO, GA 30830

CANDLER COUNTY HOSP.
ER NURSE MANAGER
P.O. BOX 597
METTER, GA 30439

CANDLER GEN. HOSPITAL
ER NURSE MANAGER
5353 REYNOLDS ST.
SAVANNAH, GA 31404

CHARLTON MEM. HOSPITAL
ER NURSE MANAGER
P.O. BOX 166
FOLKSTON, GA 31537

CLINCH MEMORIAL HOSP.
ER NURSE MANAGER
P.O BOX 516
HOMERVILLE, GA 31634

COFFEE REG. HOSPITAL
ER NURSE MANAGER
P.O. BOX 1248
DOUGLAS, GA 31533

COLLETON REGIONAL HOSP.
ER NURSE MANAGER
501 ROBERTSON BLVD.
WALTERBORO, SC 29488

DODGE COUNTY HOSPITAL
ER NURSE MANAGER
715 GRIFFIN ST.
EASTMAN, GA 31023

EFFINGHAM COUNTY HOSP.
ER NURSE MANAGER
P.O. BOX 386
SPRINGFIELD, GA 31329

EMANUEL COUNTY HOSP.
ER NURSE MANAGER
P.O. BOX 7
SWAINSBORO, GA 30401

EVANS MEMORIAL HOSP.
ER NURSE MANAGER
P.O. BOX 518
CLAXTON, GA 30417

FAIRVIEW PARK HOSPITAL
ER NURSE MANAGER
200 INDUSTRIAL BLVD.
DUBLIN, GA 31201

HAMPTON GENERAL HOSP.
ER NURSE MANAGER
P.O.B. 336
VARNVILLE, SC 29944

HILTON HEAD HOSPITAL
ER NURSE MANAGER
P.O.B. 1117
HILTON HEAD, SC 29925

JEFF DAVIS HOSPITAL
ER NURSE MANAGER
1215 S. TALLAHASSEE ST.
HAZLEHURST, GA 31539

JEFFERSON HOSPITAL
ER NURSE MANAGER
PEACHTREE ST.
LOUISVILLE, GA 30434

JENKINS COUNTY HOSPITAL
ER NURSE MANAGER
515 E. WINTHROPE AVE.
MILLEN, GA 30442

LIBERTY REG. MED. CNTR.
ER NURSE MANAGER
P.O.B. 232
HINESVILLE, GA 31313

LOW COUNTRY GENERAL
ER NURSE MANAGER
POB 400
RIDGELAND, SC 29936

MEADOWS REGIONAL MED.
ER NURSE MANAGER
POB 1048
VIDALA, GA 30474

MED. CNTR. OF CENTRAL GA
ER NURSE MANAGER
HEMLOCK ST.
MACON, GA 31208

MEMORIAL MEDICAL CENTER
ER NURSE MANAGER
4700 WATERS AVE.
SAVANNAH, GA 31406

ORANGEBORG REG.MED. CTR.
ER NURSE MANAGER
3000 ST. MATTHEWS RD.
ORANGEBORG, SC 29115

PHOEBE PUTNEY MEM HOSP
ER NURSE MANAGER
417 3RD. AVE
ALBANY, GA 31701

PIERCE COUNTY HOSPITAL
ER NURSE MANAGER
POB 32
BLACKSHEAR, GA 31516

SCREVEN COUNTY HOSPITAL
ER NURSE MANAGER
215 MIMS RD.
SYLVANIA, GA 30467

ST. LUKE'S
ER NURSE MANAGER
4201 BELFORT RD.
JACKSONVILLE, FL 32216

ST. JOSEPH'S HOSPITAL
ER NURSE MANAGER
11705 MERCY BLVD.
SAVANNAH, GA 31419

TATTNALL MEMORIAL HOSP.
ER NURSE MANAGER
RT. 1, BOX 204
REIDSVILLE, GA 30453

TELFAIR COUNTY HOSPITAL
ER NURSE MANAGER
RT. 1, BOX 5
MCRAE, GA 31055

TRIDENT REG. MED. CNTR.
ER NURSE MANAGER
9330 MEDICAL PLAZA DRIVE
CHARLESTON, SC 29418

UNIVERSITY HOSPITAL
ER NURSE MANAGER
1350 WALTON WAY
AUGUSTA, GA 30910

WASHINGTON COUNTY HOSP.
ER NURSE MANAGER
POB 636
SANDERSVILLE, GA 31082

WAYNE MEMORIAL HOSPITAL
ER NURSE MANAGER
POB 408
JESUP, GA 31545

WHEELER COUNTY HOSPITAL
ER NURSE MANAGER
3RD STREET
GLENNWOOD, GA 30428

WINN ARMY COMM. HOSP.
ER NURSE MANAGER
FT. STEWART, GA 31314

Attachment 29

MEMORIAL MEDICAL CENTER STUDIES NEW TREATMENT for PATIENTS WITH SEVERE BLOOD LOSS

Memorial Medical Center, Inc. has been asked to evaluate a new treatment for seriously injured patients admitted to its Emergency Room with severe loss of blood. The new treatment, a patented product developed by Baxter Healthcare, Inc., has potential as a blood sustitute during the emergency treatment and recovery period. Patients enrolled in the study will also receive standard treatment including blood transfusions.

The U.S. Food and Drug Administration requires new drugs and therapies to be proven effective with volunteer human patients before approval for marketing. The FDA has ruled that a patient whose life is in danger, is unable to consent, and for whom there is no one available to give consent may be given an experimental treatment when the potential benefits outweigh the risks. Patients or their families will be notified at the earliest opportunity of the patients' inclusion in the research study.

Memorial Medical Center would like to make participation in this study available to its patients who suffer from severe traumatic hemorrhagic shock, even when it is not possible to get informed consent from a family member or legal guardian prior to giving the blood substitute. Accordingly, Memorial Medical Center is taking this opportunity to communicate with the community and inform potential patients, guardians, and other appropriate parties of the potential use of this new product.

Public input is welcome. To communicate with us on this subject, please write to us at the following address:

Memorial Research Center
Memorial Medical Center
P.O. Box 23089
Savannah, Georgia 31403-3089

THE GEORGIA GUARDIAN

That much can endure and earn its place in history

August 1-7, 1997 25 CENTS

Vol. 6 No. 32

Photo by Russ Bryant

Several area physicians are at the forefront of modern medical procedures, including synthetic blood and cancer treatments.

Cutting-edge medical technology in Savannah

By Francis Zera

While some may think Savannah's small-town atmosphere may limit the availability of the newest medical treatments, several area physicians are currently offering state-of-the-art techniques to the region.

Dr. Frank Davis, Dr. John Duttenhaver and Dr. Ray Rudolph, all of whom work out of Memorial Medical Center, each offer their patients a unique form of treatment that either dramatically increases their patients' survival rates or reduces the discomfort and cost of treatment.

Memorial Medical Center's trauma center is one of only 30 hospitals nationwide that is participating in a study to test a new blood substitute, Diaspirin Cross-Linked Hemoglobin, in treating patients with serious traumatic hemorrhagic shock, which is caused by dramatic blood loss due to serious injury. Davis, as chief of trauma services, oversees the program.

The blood substitute, explained Davis, is synthesized from donated blood that has reached the end of its shelf life. "The hemoglobin molecules are taken out of the blood, linked together, diseases are eliminated, then is prepared to be frozen for up to two years." Donated accurate method for detecting potentially cancerous lumps using an in-office ultrasound device.

"Until a couple of years ago," said Rudolph, "all ultrasounds of breast tissues were done by a radiologist."

"The difference is that if you come to the office and have an abnormality but can't feel it, within 20 minutes I can tell if it's cancer or not, as opposed to waiting until the next day for traditional methods," he said. A biopsy of suspected cancerous tissues can be done with a needle, guided by an ultrasound monitor. "That way, we can talk about it right away, as opposed to putting the patient to sleep, doing a surgical biopsy, waiting for them to wake up and then trying to discuss the implications," he said. "This is much more expedient."

"There is no known cause and no known cure for breast cancer," Rudolph said. "The whole essence of breast cancer is that women who have long survival rates are the ones who have had their cancer detected early."

The best way to increase detection of breast cancer, according to Rudolph, is self-examination, regular clinical exams and annual mammograms starting at age 40.

In men, prostate cancer is as prevalent as breast cancer is in women, Duttenhaver said. It's the

The Bus Stops Here 1997-98 public school bus schedule inside this issue.

Section C.

Getting Their Feet Wet Savannah area Olympian offers inspiration to budding swimmers. Page 5A.

Complementary! SCAD painting students explore two different sides of large-format drawings. Page 1B.

Red Cross for diseases including HIV, AIDS and hepatitis. Blood used for the substitute is put through a heat process to eliminate any undetected diseases.

Among the benefits of the synthesized blood, said Davis, include its being free of blood-borne diseases, a long storage life, and, most importantly, the ability to use it with patients of any blood type. "Because you get rid of the red blood cells, there are no compatibility problems," he said.

"This is only for the sickest of the sick," explained Davis. "The people who participate in this study will be multi-system trauma victims who have lost at least 40 percent of their blood volume — only 10 or 20 patients will qualify for the study" over its one-year duration.

Based on the results of the study, the substitute could be generally available within three years. "This might not eliminate the need to give blood, but will help greatly with victims of acute trauma," he said.

Breast cancer will strike one in every nine women in the United States, and 32 percent of women who die from cancers each year die from breast cancer. In response to those statistics, vast amounts of time and money are being spent researching ways to beat breast cancer. Rudolph offers a non-invasive, men, accounting for one-third of cancers diagnosed each year.

Duttenhaver said that, in the past, the effectiveness of treatment was limited by the amount of radiation that was able to be transmitted to the cancerous gland. A new treatment called radioactive seed implant therapy holds lots of promise for increasing cure rates for this type of cancer.

"The key to curing cancer is getting the highest dose of radiation to the cancer," Duttenhaver said.

He said that prior to the introduction of implant therapy, the amount of radiation that could be used to treat prostate cancer was limited by the propensity for the organs and tissues surrounding the prostate gland to absorb excess radiation, potentially causing complications such as radiation burns.

The new technique involves introducing radioactive pellets, or seeds, into the prostate gland, precisely placing them near the cancerous tissues with a needle guided by an ultrasound monitor. The seeds are designed to emit radiation for two to six months, becoming inert within a year. "By placing the seeds precisely within the gland, we can double the dose to 16,000 rads (radiation absorbed dose, a standard radiation measure), which pushes the cure rate up to nearly 90 percent," he said.

Attachment 31

THE GEORGIA GUARDIAN
That truth can endure and earn its place in history

August 8-14, 1997/page 7A

goals for student and teacher alike. further, submitting such a paper

Letter to the Editor

MMC research coordinator expands on study policy

Thank you for the very positive article in the Aug. 1-7, 1997 Georgia Guardian, "Cutting-edge Medical Technology in Savannah."

In order to implement the protocol which Francis Zera described in his interview with Dr. Frank Davis, the FDA has approved this particular study (the use of a synthetic blood substitute in victims of severe trauma) to have "deferred consent." This means the drug can be administered immediately without the usually lengthy and intense process of obtaining consent from the patient or family. The administration of the diaspirin drug must be finished within 60 minutes of the patient arriving in the emergency room, and there are numerous lab and other diagnostic procedures to be completed before the administration of the drug product. Also, on many occasions, unresponsive or otherwise not responsible patients arrive at the ER alone and without clear information on how to contact their families immediately.

Therefore, the FDA has granted this special privilege (of deferring the consent process) to Memorial Medical Center and the other hospitals participating in the study, with the proviso that informed consent will be obtained as soon as possible. With these "total body crunch" patients who have suffered severe, multiple trauma with hemorrhage, this almost always means that the responsible family member will be the person to sign the form, after being comprehensively advised of benefits and risks by one of the physicians in the study.

This responsible person has the unimpeded choice at that time to state that the study may not continue and he or she is so advised that this decision will be honored immediately without prejudicing any other alternative treatments or affecting the patient's care in any adverse manner. Of course, the responsible person also has the choice to allow the patient to continue in the study. The procedures after the initial administration of the drug are no more than "following" the patient to see how his or her condition fares for the following 28 days after admission. Some lab work is involved, but charges for these tests, as well as for the drug itself, are paid for by the sponsoring drug company, Baxter Laboratories. Administration of the drug is not, under any circumstances, repeated after the initial dosage.

Earl Stanford, RN BSN CCRC
Certified Clinical Research Coordinator
Research Center
Memorial Medical Center

Attachment 32

Newscast, July 15, 1997
Channel 3, WSAV, NBC affiliate
Savannah, GA

Introduction: News anchors introduced product as a "...new blood substitute which can save lives. Some experts believe it may be better than the real thing."

Segway to Family Health Reporter, Kristin Hill at " Memorial Medical Center where the product is being tested."

Kristin Hill: "You're rushed into the emergency room with a serious injury. You've lost a lot of blood and are going into shock. You need blood fast but typing and checking for antibodies takes time. Using a new blood substitute made from outdated blood could save time and your life."

Dr. Gage Ochsner, Chief of Trauma Services, Memorial Medical Center explains: "The solution is given through the vein and early on. Patients who get this are given it within 30 minutes of arrival."

Kristin Hill: "When Life Star (helicopter) or an ambulance brings in a trauma patient, using the blood substitute can save critical amounts of time because blood typing is not necessary and the blood product can be stored in the emergency room. Memorial Medical Center is taking part in National test trials."

Dr. Ochsner: "We will be giving solution to patients who have a 40% chance of dying or greater because of blood loss."

Kristin Hill: "Memorial will enroll 10-20 patients in the study. Prior consent is not required by FDA for a patient to receive the blood solution."

Dr. Ochsner: "FDA has authorized use because of the potential benefit of using this outweighs the risk associated with it."

Kristin Hill explains: As the blood substitute carries oxygen to cells and tissues it increases blood flow to vital organs just like real blood, but keeps longer, and when given with real blood it may mean better survival rates and fewer complications for trauma patients.

Closing: Program ends with the following message. "For more information on the study call Memorial Medical Center Trauma Research Study, Phone number 912 350-8707."

Attachment 33

Clinical Trial of Diaspirin Cross-Linked Hemoglobin
Emergency Treatment of Patients in Shock

Memorial Medical Center is among 35 major trauma centers that are evaluating a new treatment for critically injured patients with severe blood loss. The treatment involves administering an experimental blood product to such patients, who face a major risk of dying despite the best medical care. Baxter Healthcare, Inc., has developed the product, Diaspirin Cross-linked Hemoglobin (DCLHb™), which is being tested during the emergency treatment of trauma patients in shock. The trial, which is authorized by the U.S. Food and Drug Administration, requires public notice because it will occur under emergency conditions that may require an exception from informed consent. The following is to help to prepare you to answer potential questions about the trial.

Q. Why is this trial being performed?

A. Seriously injured patients frequently arrive at the hospital in shock with significant blood loss. Despite the best care medicine has to offer, as many as 40 percent of the most critically injured patients will die from their injuries. Studies suggest that DCLHb™ may improve the chance of survival following severe blood loss. The product has the greatest chance of improving survival and reducing complications when it is given immediately after the beginning of catastrophic shock and bleeding.

Q. What is DCLHb™?

A. DCLHb™ is a purified hemoglobin (the part of blood that carries oxygen) preparation made from human blood that has become outdated on blood bank shelves and is no longer usable for transfusions. It is filtered and heated to reduce the risk of blood-borne infections including AIDS. DCLHb™ may restore blood pressure, increase blood flow to vital organs and carry oxygen to cells and tissues. Because blood typing is not required and the product can be stored in the Emergency Department, DCLHb™ can be given immediately after a patient's arrival, saving critical moments in stabilizing a trauma-patient.

Q. Does DCLHb™ replace the need for blood transfusion?

A. DCLHb™ is administered in addition to transfusions that may be needed to treat the injured patient. (Since the product is made from human blood, it would not be suitable in treating patients whose religious beliefs forbid blood transfusions.) Patients will still get all standard therapies in this study, including blood, fluids and surgery. Although DCLHb™ may reduce the number of blood transfusions required to treat the injured, volunteer blood donations are still vital.

Q. What is an exception from informed consent and why is it necessary?

A. Because trauma patients are often so severely injured, they may not be able to give their consent to participate in the drug trial. Still, they are in critical need of immediate treatment. The U.S. Food and Drug Administration has granted an exception from informed consent in such cases. They have carefully evaluated DCLHb™ and determined that the potential benefits greatly outweigh the risks of participating in the trial. As a result, patients may be enrolled in this study and receive DCLHb™ when informed consent is not possible.

We will make every attempt to obtain consent from patients, their legal representatives, or family before DCLHb™ is given, and all patients and their family members will be completely informed of their participation as soon as possible. At all times, the patient or their representatives may decline further participation in the study. There are no known risks to patients who decide not to continue in the study.

Q. What are the risks and side effects of DCLHb™ ?

A. DCLHb™ has been extensively studied in randomized trials involving more than 700 patients over a four-year period to evaluate its effects. Of the approximately 350 who received the drug, a few temporary side effects were noted. These included changes in some lab test results, a temporary and harmless yellowing of the skin (unrelated to liver damage), temporary reddening of the urine due to the red color of DCLHb™, nausea, and back, abdominal and muscle pain. Blood pressure may be elevated following administration; however, this may be beneficial to patients in shock, whose blood pressure is dangerously low. Independent experts will monitor patient safety throughout the trial.

Q. Who will be eligible to participate?

A. Approximately 30 patients with low blood pressure and in shock from blood loss following traumatic injury will be enrolled at Memorial over the next 18 months. Approximately half of these patients will receive the blood product along with other treatment. This product will be given only to patients who have such major blood loss that standard therapy may not be enough to save their lives. A total of 850 patients will be enrolled nationwide at 35 trauma centers. No additional charges will be incurred by patients as a result of participation.

Attachment 34

For June 16 Notations to physicians:

Dr. Raymond P. Bynoe, Trauma Services, will serve as principal investigator in a study on Diaspirin Cross-Linked Hemoglobin that will begin by August. DCLHb, a man-made hemoglobin solution, will be used in patients suffering traumatic shock from blood loss. Dr. N. John Stewart of Emergency Services will join Bynoe as co-investigator in the study.

RMH is one of 40 hospitals nationwide, and the only one in South Carolina participating in the study. A maximum of 20 patients will be eligible to participate in the study during the next 12 months. For more information, call 434-6418.

FOCUS

Richland Memorial Hospital VOLUME 24 NUMBER 7 JULY 8, 1997

New treatment to be tested at RMH

RMH is one of 40 hospitals nationwide and the first in South Carolina that will begin using a potentially life-saving treatment in August for patients h severe traumatic injury. The ıtment being researched is made from nan red blood cells and is called ıspirin Cross-Linked Hemoglobin ⊃LHb).

"The purpose of the study is to find how well the new hemoglobin ıtion works in treating or preventing harmful effects of blood loss due to er ry, including shock, severe e death," says Dr. Raymond noe, medical director of Trauma vices and principal investigator of the dy. "We hope the use of this product as pplement to our life-saving cedures will improve patient comes.

"Despite our best efforts, about percent of trauma patients with remely low blood pressure die, most of m from bleeding problems. Large ounts of blood loss can result in lack of gen to vital tissues, which can lead to ltiple organ failure. DCLHb may rease blood flow and oxygen to the organs, helping stabilize a ient quicker. Patients in this study still will receive all standard rapies, including blood products, fluids, medications and surgery."

DCLHb is a purified hemoglobin solution, the part of blood that ries oxygen throughout the body. The solution is made from red od cells donated by healthy volunteers who have been tested and nd negative for the viruses that cause hepatitis and AIDS. In lition, DCLHb solution goes through a specialized filtration and pasteurization process to significantly reduce the risk of viral transmission. Because the product is made from human blood cells, it will not be suitable for treating patients whose religious beliefs forbid blood transfusions.

George Fulton

RMH will begin using a potentially life-saving treatment next month for patients with severe traumatic injuries.

"While we're excited about the possibility of this research increasing the survivability of trauma patients, we also are excited about it possibly extending the community's blood supply," says Dr. John Stewart, director of Emergency Services and co-investigator in the research project. "This could help extend our resources nationwide."

The study, which is authorized by the U.S. Food and Drug Administration (FDA), will be randomized. This means half the participants will receive the solution and half will receive saline solution after receiving all standard therapies. Neither the patient nor the doctor will know which solution the patient has been given.

The study will be monitored by an independent data monitoring committee. Trauma patients must meet strict criteria before being given the new treatment. Part of the inclusion criteria includes being 18 years of age or older, evidence of hemorrhage, and low blood pressure. Of the 1,500 patients Trauma Services treats each year, approximately 20 patients will be eligible to receive the new product in the next 12 months through the study.

Employees are invited to attend a news conference about DCLHb at 10:30 a.m., July 8, in Dining Room B.

For more information, call Trauma Services at 6418. ■

EMIER PURCHASING PROGRAM STRENGTHENS UALITY, IMPROVES COST EFFECTIVENESS

Strengthening quality and improving cost effectiveness are mmitments RMH states in its vision statement. One such way contract prices."

According to Garvin, there are some exceptions, such as when

News Release Focus

New Treatment to be Tested at RMH

RMH is one of 40 hospitals nationwide and the first in South Carolina that will begin using a potentially life-saving treatment in August for patients with severe traumatic injury. The treatment being researched is made from human red blood cells and is called Diaspirin Cross-Linked Hemoglobin (DCLHb).

"The purpose of the study is to find out how well the new hemoglobin solution works in treating or preventing the harmful effects of blood loss due to severe injury, including shock, severe illness or death," says **Dr. Raymond Bynoe**, medical director of Trauma Services and principal investigator of the study. "We hope the use of this product as a supplement to our life-saving procedures will improve patient outcomes.

"Despite our best efforts, about 40 percent of trauma patients with extremely low blood pressue die, most of them from bleeding problems. Large amounts of blood loss can result in lack of oxygen to vital tissues, which can lead to multiple organ failure. DCL Hemoglobin may increase blood flow and oxygen to the organs, helping stabilize a patient quicker. Patients in this study still will receive all standard therapies, including blood products, fluids, medications and surgery."

DCL Hemoglobin is a purified hemoglobin solution, the

part of blood that carries oxygen throughout the body. The solution is made from red blood cells donated by healthy volunteers that have been tested and found negative for the viruses that cause hepatitis and AIDS. In addition, DCL Hemoglobin solution goes through a specialized filtration and pasteurization process to significantly reduce the risk of hepatitis and AIDS. Because the product is made from human blood cells, it will not be suitable in treating patients whose religious beliefs forbid blood transfusions.

"While we're excited about the possibility of this research increasing the survivability of trauma patients, we also are excited about it possibly extending the community's blood supply," says Dr. John Stewart, director of Emergency Services and co-investigator in the research project. "This could help extend our resources nationwide."

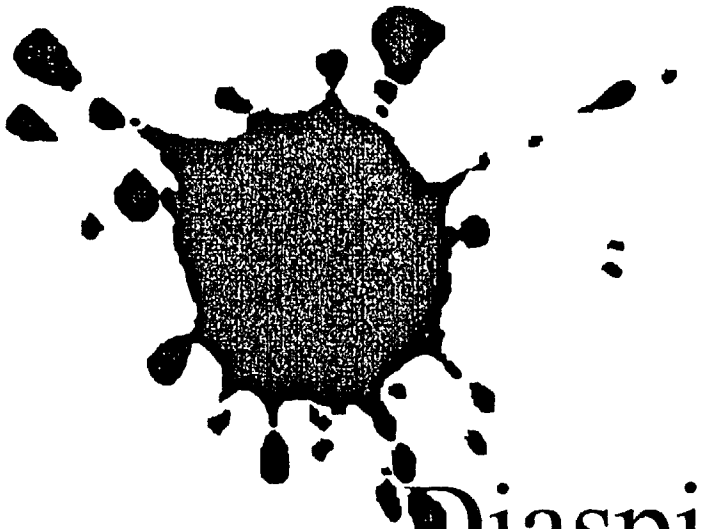
The study, which is authorized by the U.S. Food and Drug Administration (FDA), will be randomized. This means half the participants will receive the solution and half will receive saline solution. Neither the patient nor the doctor will know which solution the patient has been given. The study will be monitored by an independent data monitoring committee.

Trauma patients must meet strict criteria before being given the new treatment. Part of the inclusion criteria includes being 18 years of age or older, evidence of hemorrhage, and low blood pressure. Because of this, out of

the 1,500 patients Trauma Services treats each year, Bynoe says only a maximum of 20 patients will be eligible to receive the new product in the next 12 months through the study.

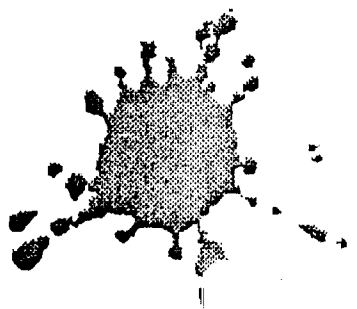
For more information, call Trauma Services at 6418.

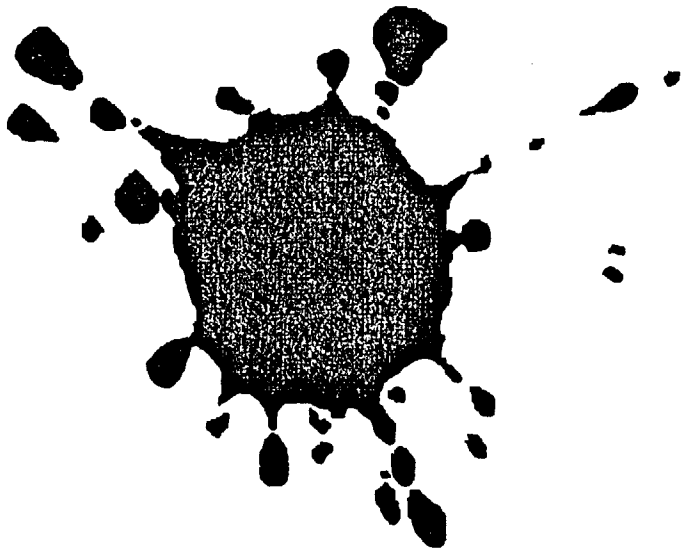
Attachment 36



Diaspirin Cross-Linked Hemoglobin (DCLHb)

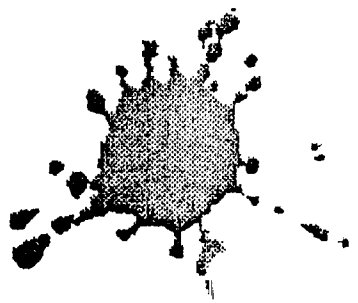
Utilization in the treatment of severe traumatic hemorrhagic shock





Objective

Whether the infusion of DCLHb will reduce the mortality following traumatic hemorrhagic shock



Informed Consent

- FDA approved exception to consent
  - notification of next of kin, legal guardian
- Critically short therapeutic window
- Direct benefit to patients
- IRB
- Notification of Medical community
- Community Education/Information

Randomized Prospective Study

Group One	Group Two
Blood Products plus Placebo	Blood Products plus DCL-Hg

000-000178

Trauma Services - RMH

DCLHb

- Prepared from volunteer donor red cells
- Final 10 % solution
  - contains 10 g of hemoglobin per 100 ml.
  - iso-osmotic with whole blood
  - hyperoncotic
  - adjusted to a pH of 7.4 at 37 degrees C

The 500-1000 ml. study dose provides 50 -100 g of hemoglobin

Inclusion Criteria

- 18 years of age or older
- Evidence of hemorrhage
- Tissue hypoxia & cellular hypoperfusion
  - SBP 90 or less and HR 120 or above OR
  - SBP 90 or less and HR 60 or less with a preterminal rhythm(junctional or idioventricular) OR
  - Base deficit of 15 mmol/L or worse

Exclusion Criteria

- Age less than 18
- Known pregnancy
- Pulseless traumatic arrest during hospitalization
- Imminent death precludes resuscitation efforts
- Isolated head injury, penetrating or blunt
- Known objection to use of blood/blood products
- Known injury time >4 hrs. prior to infusion
- Combined multisystem and head trauma with clinical findings consistent with significant mass effect(e.g.,severe coma, lateralizing signs, posturing or pupil dilation secondary to uncal herniation)
- Hospitalization > 60 min prior to infusion

000-000182

End Points

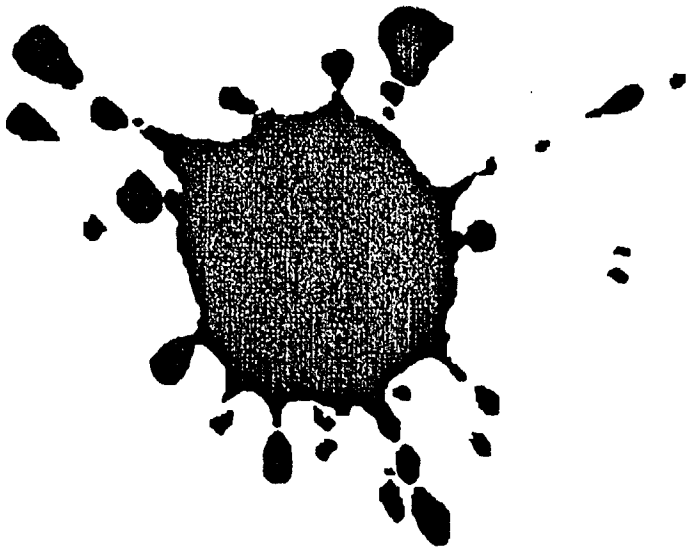
- Primary - Statistically significant reduction in 28 day mortality
- Secondary- 48 hour mortality reduction and Lactate level

DCL Hb Effects

- Increase in mean arterial pressure
  - Dose related response
- Increase organ perfusion
  - Restoration of acid/base balance
- Decreased bacterial translocation
- ? Decrease use of banked blood products

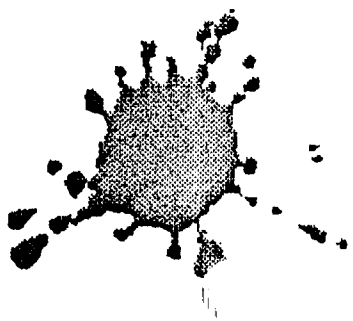
DCL Hb PREPARATION

- Human volunteer blood
- Tested and found negative for HBsAg, HIV-I/II & HCV
- Red cells lysed to release hemoglobin
- Ultrafiltration & reacted with diaspirin x-linked agent
- Stabilized tetrameric hemoglobin
- Pasteurization to effect viral deactivation
- Solution conc. into physiologic vehicle
- Similar to process used to prepare albumin



DCL Hb

HEMOGLOBIN
CONCENTRATION OF PRBC's
20 GM/DL

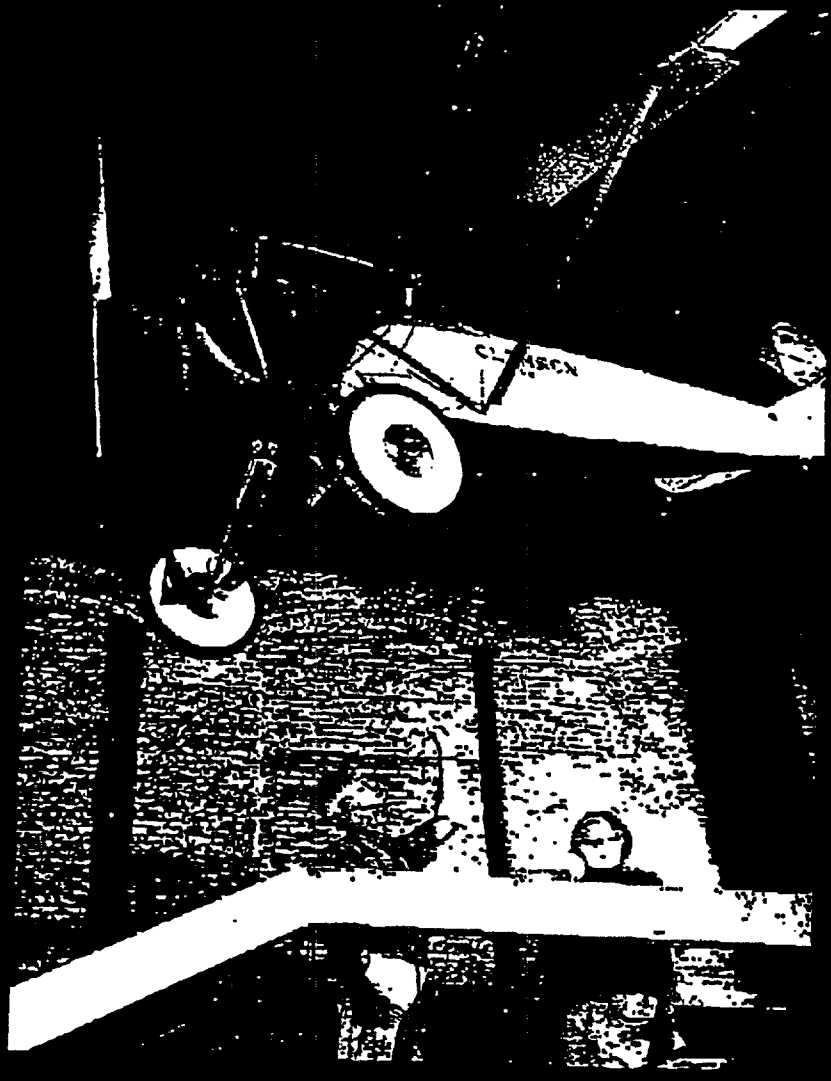


Attachment 37

000-000187

The Recorder

Columbia Medical Society of
Richland County, S.C., Inc.
COLUMBIA, S.C.



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The Recorder

Columbia Medical Society of Richland County, S.C., Inc.

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CONTENTS

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Classified Ads: Minimum member rate is $10, non-members $15. Call the Columbia Medical Society office (803-765-1498) for rate information.

The Efficacy Trial of Diaspirin Cross-Linked Hemoglobin (DCLHb) in the Treatment of Severe Traumatic Hemorrhagic Shock

by Raymond P. Bynoe, M.D.

Trauma is the leading cause of death in Americans between the ages of 1 and 44 years, and is surpassed only by cancer and atherosclerosis as a cause of death in all age groups. Approximately 60 million injuries occur each year, and at least half of these people require medical care; of these 30 million injuries, 3.6 million require hospitalization. Trauma is responsible for 145,000 deaths in the USA each year, frequently from shock that is refractory to resuscitation efforts.

The Trauma Service of Richland Memorial Hospital is excited to be able to inform the medical community about the Service's participation in a multi-centered efficacy study about Diaspirin Cross Linked Hemoglobin (DCLHb). DCLHb is a purified human hemoglobin solution that can be utilized in the treatment of severe traumatic hemorrhagic shock. This solution, unlike traditional blood products, does not require cross-matching, and is thus immediately available for infusion in the trauma resuscitation. Blood that has been screened for HIV and Hepatitis viruses is heated and filtered during the pasteurization process to make DCLHb.

DCLHb, in the preliminary studies, has been shown to effectively transport oxygen in vivo as demonstrated by a P50 equal to that of pure human red blood cells. DCLHb has also been shown to optimize vital organ blood flow, prevent tissue hypoxia and lactic acidosis, and ultimately improve survival. DCLHb has also been shown to be effective in small volumes, and thus may improve perfusion in the trauma patient without the untoward effects of large volume crystalloid infusions.

Patients can be enrolled in this efficacy trial if they demonstrate severe shock with signs of hypoperfusion. Patients such as these have a projected mortality rate of 40%. The primary purpose of this study will be to determine whether this infusion can reduce 28 day morbidity and mortality following traumatic hemorrhagic shock.

Approximately twenty patients will be enrolled in the study at RMH over a 12 month period, with at least 800 enrolled in 40 centers nationwide. For additional information on this very promising new solution, please contact Dr. Raymond Bynoe, Dr. Richard Bell or Jay Hamm, RMH Trauma Coordinator, at 434-6418.

VOLUNTEERS NEEDED FOR CMS PROGRAMS

Please call the Society office if you are willing to take part in any of these Society programs:

Mini-Internship Program (see P.14)

Mentoring Program for USC Medical and Pre-Med Students

Anti-Violence Program for at risk school children

Judge entries for CMS awards at the SC Region II Science Fair

For more information call CMS at 765-1498

Attachment 38

June 30, 1997

Community Leader

Dear ,

It is important to recognize that trauma, no matter the cause, has a very high mortality rate and is the leading cause of death for people aged 1-44 years. Trauma is surpassed by only cancer and atherosclerosis as a leading cause of death among all Americans. Approximately 60 million injuries occur each year. At least half of these people require medical care and of the 30 million injured people, 3.6 million have to be hospitalized. Richland Memorial Hospital evaluates over 14,000 patients involved in trauma in the Midlands of South Carolina each year with approximately 1500 admissions.

Trauma is responsible for 145,000 deaths in the United States each year. A major portion of these deaths occur within the first hour following the traumatic event. Many of these deaths are associated with the inability to restore the blood pressure (shock). Despite recent medical and surgical advancements, treatment of life-threatening shock from blood loss secondary to trauma is not always successful.

Trauma Services of Richland Memorial Hospital is excited to announce its participation in a Federal Drug Administration (FDA) approved efficacy trial of Diaspirin Cross-Linked Hemoglobin (DCLHb™) in the treatment of severe traumatic hemorrhagic shock. DCLHb™, a Baxter Healthcare product, is a purified hemoglobin solution made from human blood.The potential advantages of DCLHb™ are: 1) it does not have to be matched to the patient's blood type, 2) it is immediately available for infusion in trauma patients, and 3) it transports and unloads oxygen to the body's cells. The processing of this product effectively reduces the risk of AIDS and other infectious diseases. Testing for carcinogencity for DCLHb™ was not necessary because it is a biological formulation of natural blood protein. Blood, or its products, have never been implicated in causing cancer.

Patients that will be included in the study are trauma patients that have an extremely low blood pressure, (Class III or IV Hemorrhagic Shock) secondary to car or motorcycle crashes, gunshot wounds, stabbings, assaults, or falls. Exclusion criteria include age less than 18 years, pregnancy, or closed head injury. The study will help determine the effectiveness of DCLHb™ in this trauma patient population. All trauma patients enrolled in the study will receive, along with the study solution, all current standard or usual treatments for shock. This may include intravenous solutions, blood and/or blood products, medications, or surgery.

Due to the severity of their injuries, most patients will be unable to give informed consent to participate in this valuable project. However, every effort will be made to obtain informed consent as soon as possible from either the patient or next of kin. The next of kin or legal guardian may withdraw the patient from the study at any time. This procedure follows the FDA's " Exception from Informed Consent Requirements for Emergency Research", #21 CFR 50.24.

Our participation along with 39 other hospitals will give the FDA the appropriate scientific data to evaluate the effectiveness of this new solution, DCLHb™. The study will be monitored by an independent safety group which is not affliliated with Baxter Healthcare or Richland Memorial Hospital. Approximately twenty (20)

trauma patients will be enrolled in this efficacy study at Richland Memorial Hospital over a 12 month period, with at least 850 patients enrolled at the 40 centers nationwide.

In light of an ongoing nationwide blood shortage, Trauma Services of Richland Memorial Hospital sincerely feel that DCLHb™ will not only benefit patients enrolled in the study but will offer a significantly improved chance of survival for many more trauma patients in the future. For additional information on this very promising new solution, please contact Dr. Raymond Bynoe, Dr. John Stewart, or Jay Hamm, R.N. at 803-434-6418. In addition, you are invited to attend a press conference on Tuesday July 8, 1997, in Dining Room B of Richland Memorial Hospital, at 10:30 am.

Sincerely,

Raymond Bynoe, MD, FACS
Medical Director, Trauma Services

N. John Stewart, MD, FACEP
Medical Director, Emergency Medicine

Vince Ford
Vice President, Community Services

The Efficacy Trial of Diaspirin Cross-Linked Hemoglobin(DCLHb) in the Treatment of Severe Traumatic Hemorrhagic Shock

Trauma is the leading cause of death in Americans between the ages of 1 and 44 years and is surpassed only by cancer and artherosclererosis as a cause of death in all age groups. Approximately 60 million injuries occur each year and at least half of these people require medical care; of these 30 million injuries, 3.6 million require hospitalization. Trauma is responsible for 145,000 deaths in the USA each year, frequently from shock that is refractory to resuscitation efforts.

The Trauma Service of Richland Memorial Hospital is excited to be able to inform the medical community about the Service's participation in a multi-centered efficacy study about Diaspirin Cross Linked Hemoglobin (DCLHb). DCLHb is a purified human hemoglobin solution that can be utilized in the treatment of severe traumatic hemorrhagic shock. This solution, unlike traditional blood products, does not require cross-matching and is thus immediately available for infusion in the trauma resuscitation. Blood that has been screened for HIV and Hepatitis viruses is heated and filtered during the pasteurization process to make DCLHb.

DCLHb, in the preliminary studies, has been shown to effectively transport oxygen in vivo as demonstrated by a P50 equal to that of pure human red blood cells. DCLHb has also been shown to optimize vital organ blood flow, prevent tissue hypoxia and lactic acidosis, and ultimately improve survival. DCLHb has also been shown to be effective in small volumes, and thus may improve perfusion in the trauma patient without the untoward effects of large volume crystalloid infusions.

Patients can be enrolled in this efficacy trial if they demonstrate severe shock with signs of hypoperfusion. Patients, such as these, have a projected mortality rate of 40%. The primary purpose of this study will be to determine whether this infusion can reduce 28 day morbidity and mortality following traumatic hemorrhagic shock.

Approximately twenty patients will be enrolled in the study at RMH over a 12 month period, with at least 800 enrolled in 40 centers nationwide. For additional information on this very promising new solution, please contact Dr. Raymond Bynoe, Dr. Richard Bell or Jay Hamm, Trauma Coordinator, at 434-6418.

Trauma Research Study

* Research led by Dr. Raymond Bynoe, Dr. Richard Bell, Stan Fowler of USC and Trauma Services. Expected to begin the end of July or beginning of August.

* RMH is one of 40 sites nationwide.

* Research is using a derivative of human blood products. Will use with patients who have traumatic blood loss and shock. Recipients will have to meet strict criteria. There will be about 1-2 patients per month who will receive the product.

* The product will be given to these patients because they have a high mortality rate, and this product may help them by increasing the body's ability to deliver oxygen to it's cells.

* Secondarily, another benefit may be the possibility that use of the product can extend the community's blood supply.

* We will be informing the community of the study through letters to community leaders and special interest groups and through a press conference either the end of June or beginning of July.

* In other areas, there were a few community concerns about using an "artificial" blood product. This is not an artificial product, it contains human components. Jehovah witnesses can't receive it.

* Another concern to be aware of is the consent process. As in any trauma situation, consent to use the product will be sought from family members, however, the trauma team will use whatever it can to help a person survive. And, that may include use of this product.

* For questions, call Dr. Bynoe's office at 6418.

Questions and Answers
Richland Memorial's Trauma Research Study

Why is this study being performed?

Seriously injured patients frequently arrive at the Trauma Center in shock and suffering from significant blood loss. The purpose of this study is to find out how well the new hemoglobin solution works in treating or preventing the harmful effects of blood loss due to severe injury, including shock, severe illness or death. Approximately 850 patients will take part in this study at 40 hospitals nationwide. Richland Memorial is the first hospital in South Carolina to participate.

What is Diaspirin Cross-Linked Hemoglobin (DCLHb)?

Diaspirin Cross-Linked Hemoglobin is a purified hemoglobin, the part of the blood that carries oxygen. It is made from red blood cells donated by healthy volunteers that have been tested and found negative for the viruses that cause hepatitis and AIDS. In addition, DCLHb solution goes through a specialized filtration and pasteurization process to significantly reduce the risk of hepatitis and AIDS. Because the product can be stored in the Emergency Department, it can be given immediately after a patient's arrival, saving critical moments in stabilizing a trauma patient.

How is the study conducted?

The study is randomized, meaning half the participants will receive the solution and half will receive saline solution. Neither the patient nor the doctor will know which solution the patient will be given. This treatment will be given in addition to standard therapies, not in place of. The trial is authorized by the U.S. Food and Drug Administration (FDA), and will be monitored by an independent data monitoring committee.

Does this replace blood transfusions in the critically injured trauma patient?

No. DCLHb is administered in addition to transfusions that may be needed to treat a patient. Since this product is made from human blood cells, it would not be suitable in treating patients whose religious beliefs forbid blood transfusions. Patients in this study will receive all standard therapies, including blood products, fluids, medications and surgery.

Who will be chosen to participate in this study?

Approximately 20 patients will participate in the study. There is strict medical criteria that the physicians will follow to ensure a patient may participate. Part of the inclusion

criteria includes being 18 years of age or older, evidence of hemorrhage and low blood pressure.

How will a patient know if he or she is receiving the treatment?

Informed consent will be sought from patients if they are conscious and able to make a decision, and/or by family members who will be contacted. Every attempt will be made to obtain consent from the patients, their families or legal representatives before the treatment is given. As with any trauma situation, when a patient is in critical need of immediate attention, the physician will do what is necessary to help the patient survive.

The Food and Drug Administration (FDA), in cooperation with the National Institutes of Health (NIH), issued regulations that allow for certain emergency research to be conducted with an exception from informed consent in rare circumstances when the patient cannot provide consent and the nature of the patient's medical condition requires immediate attention. This study will fit into that criteria. These regulations allow for the advancement of vital emergency research with careful attention to the protection of the rights and welfare of the patients who are enrolled in the study. The FDA and NIH expect that the studies conducted under these rules will allow patients in certain life-threatening situations, who are unable to give informed consent because of their condition, the chance to receive potentially life-saving treatments.

What are the risks and side effects of the treatment?

The product has been extensively studied in randomized trials involving more than 700 patients over a four-year period to evaluate its side effects. Of the approximately 350 patients who have received the treatment, a few temporary side effects were noted, including: temporary and harmless yellowing of the skin, temporary reddening of urine due to the red color of the product, nausea, and back, abdominal and muscle pain.

Who should I contact if I have questions?

If at any time you have questions about the research study, call Dr. Raymond Bynoe, Dr. John Stewart or Jay Hamm of Trauma Services at 434-6418.

Attachment 39

FOR MORE INFORMATION
CONTACT JO HALMES
OR TAMMIE EPPS
PUBLIC RELATIONS, 434-6891

FOR IMMEDIATE RELEASE
June 26, 1997

New, potentially life-saving treatment to be tested at Richland Memorial Hospital

COLUMBIA, S.C. -- Richland Memorial Hospital is one of 40 hospitals nationwide that will begin using a potentially life-saving treatment for patients with severe traumatic injury. The treatment will be available for use beginning in August for patients with severe blood loss secondary to traumatic injuries.

The treatment being researched, Diaspirin Cross-Linked Hemoglobin (DCLHb), is made from human red blood cells.

"We hope the use of this product as a supplement to our life-saving procedures will improve patient outcomes," says Dr. Raymond Bynoe, medical director of Trauma Services and principal investigator of the study. "Despite our best efforts, about 40 percent of trauma patients with extremely low blood pressures, secondary to bleeding problems, die. Large amounts of blood loss can result in lack of oxygen to vital tissues, which can lead to multiple organ failure several days or weeks after the initial trauma.

"DCLHb may increase blood flow and oxygen to vital organs. It also may help us stabilize a patient with severe blood loss."

The DCLHb solution goes through a specialized filtration process to remove hemoglobin, the oxygen-carrying component of the blood. The product is then pasteurized to significantly reduce the risk of viral transmission. Trauma patients must meet strict criteria before being given the new product.

Trauma Services at Richland Memorial treats about 1,500 patients per year. Approximately 20 trauma patients will be eligible to receive the new product in the next 12 months through the study.

"Due to the severity of their injuries, most of these patients will be unable to give informed consent to participate in this valuable project," Bynoe says. "However, every effort will be made to obtain informed consent as soon as possible from either the patient or next of kin. The next of kin or legal guardian may withdraw the patient from the study at any time. This procedure follows the FDA's 'exception from informed consent requirement for emergency research.'"

Bynoe is joined in his research by Dr. N. John Stewart, director of Emergency Services and co-investigator.

"While we are excited about the possibility of this research increasing the survivability of trauma patients, we also are excited about it possibly extending the community's blood supply," Stewart says. "This could help extend our resources nationwide."

If community members are interested in more information about the research project, they may call Trauma Services at 434-6418.

# # #

ERIK CAMPOS/THE STATE

State Treasurer Richard Eckstrom, left, and Comptroller General Earle Morris have apparently ended their 'feud' and cordially joked with other members of the state Budget and Control Board on Tuesday. 'Happy days are here again,' Gov. David Beasley said.

Eckstrom, Morris make peace

"The feud is over; there is no feud. It takes two to feud. And I'm not going to feud. We'll work together. He's a very good man."

STATE TREASURER RICHARD ECKSTROM

By MICHAEL SPONHOUR
Staff Writer

State Treasurer Richard Eckstrom and Comptroller General Earle Morris didn't exactly kiss or hug, but they did call a halt Tuesday to their heated feud.

The rivals shook hands before the opening of the regular meeting of the state Budget and Control Board. They even chatted and shared a laugh.

That's quite a turnaround from last month, when the two men tore each other limb from gut in the media.

"The feud is over; there is no feud," Eckstrom said. "It takes two to feud. And I'm not going to feud. We'll work together. He's a very good man."

The spat has been "media-driven," said Morris, the highest-ranking Democrat in state government.

"Let's end this silliness," he said. "In 45 years, I've gotten along with every elected official in South Carolina. The problem is not me."

In June, Eckstrom called Morris a declining old man gripped by hatred and petty jealousies. Eckstrom said Morris had made an obscenity-laced call to Eckstrom's house late one night after finding out that Eckstrom had removed the comptroller's signature from state checks.

Eckstrom also charged that aides to Morris had spat upon and put chewed gum near his car in the State House garage.

Morris denied those allegations and charged that the first-term Republican was a self-promoter trying to distract attention from a sexual harassment investigation.

Former Eckstrom spokeswoman Leann Register-Johnson has filed a complaint with the Human Affairs Commission charging that she was given poor job evaluations for resisting Eckstrom's attempt to kiss her in January 1996.

Just to make sure peace is maintained, Gov. David Beasley met with the two men privately Tuesday.

"He said to be sweet and kind and to love everybody," said Morris, who still insists that his signature should be on state checks.

Beasley urged the two to give up their ugly feud for the good of the state, said spokesman Gary Karr.

"It's best for both of them to put the past and whatever disputes they have had behind them and to work together whenever they can," Karr said. "These are both good men who have done a lot of good work for South Carolina."

"Let's end t silliness. In years, I've gotten alon with every elected offic in South Carolina."

COMPTROLLER GENE EARLE MORRIS

Richland Memorial to test blood substitute on 20 patients

By LEVONA PAGE
Senior Writer

Over the next year, 20 patients in Richland Memorial Hospital's emergency room will help test a new blood substitute that could eventually relieve worries about tainted transfusions and supply shortages.

The substitute, called Diaspirin Cross-Linked Hemoglobin, will not be used totally instead of normal blood transfusions, but will be used to supplement them.

Patients who will get the blood substitute during the test period are those likely to bleed to death without it, said Dr. Raymond Bynoe, medical director of Trauma Services and principal researcher.

By not having to match blood types or scurry for blood supplies, time can be saved, Bynoe said. "What we are trying to do is help patients who are a high risk for death."

The blood substitute, made by Baxter Healthcare Corp., is a highly filtered and pasteurized hemoglobin, the part of the blood that carries oxygen. The product is made from red blood cells of healthy donors.

A main function of normal blood is to carry oxygen to the vital organs and throughout the body. Because the blood substitute is rich in oxygen, less normal blood would be needed, Bynoe said.

"Instead of using five or six units of blood, we might use two or three," he said. "This will expand our blood supply."

The substitute also could decrease the risk of getting the AIDS virus or hepatitis through blood transfusions because the extra filtering and pasteurization will remove contamination, Bynoe said.

"These additional processes will decrease the risk substantially," he said.

The 20 patients who help test the product might not know in advance that they doing so. When possible, patient or fa consent will be sought, but federal Food Drug Administration rules adopte November allow hospitals to proceed in ous emergencies without consent.

The FDA approval acknowledged that first hour of treatment is crucial in se trauma cases, Bynoe said.

"This is known as the golden hour, we have to be very, very, very aggressiv this time period," he said.

PLEASE SEE **BLOOD** PAGE

BLOOD

FROM PAGE B1

Patients chosen for the test must be at least age 18, have evidence of hemorrhage and low blood pressure, no evidence of pregnancy and no head injury. They will be observed for at least 28 days after the procedure.

Risks are believed to be small, although the FDA has some concerns about the substitute causing hypertension or altered blood flow. Previous trials have produced a few temporary side effects such as yellowing of the skin, reddening of the urine, nausea or pain in the back, abdomen or muscles.

All liability from potential risk is being assumed by Baxter, Bynoe said. Richland is one of 40 hospitals nationwide and the only one in South Carolina participating in the tests, which are to begin in August. Bynoe's partner in the research is Dr. John Stewart, director of Emergency Services at Richland.

About 40 percent of the patients nationwide, or 140,000 to 160,000 people, who enter emergency rooms after severe trauma ultimately die, Bynoe said. If that number can be reduced by 10 percent by using the blood substitute, a significant number of lives will be saved, he said. The search for a substitute for blood goes back to the 17th century, with researchers trying animal blood and wine.

Levona Page can be reached at 771-8512 or by fax at 771-8430.

Attachment 41

000-000201

25

A News Clip From:
Morning News
Florence S.C.
Circ: 33,000
Date of Clip:

JUL - 9 1997

S.C. Press Services Clipping Bureau

New trauma treatment to be tested at Columbia

25

COLUMBIA — Some trauma patients at Richland Memorial Hospital will be getting a new blood product that doctors hope will save lives by providing more of the blood's vital oxygen-carrying component.

The hospital said Tuesday it is one of 40 in the nation testing what is called Diaspirin Cross-Linked Hemoglobin.

Through filtering and pasteurization, the solution concentrates hemoglobin, the blood component that carries oxygen to the body's tissues, while reducing the risk from other blood-borne infections.

Johns Island has

25

A News Clip From:
The Post & Courier
Charleston S.C.
Circ: 110,833
Date of Clip:

JUL - 9 1997

S.C. Press Services Clipping Bureau

Trauma center tries new blood product

25

Associated Press

COLUMBIA — Some trauma patients at Richland Memorial Hospital will be getting a new blood product that doctors hope will save lives by providing more of the blood's vital oxygen-carrying component.

The hospital said Tuesday it is one of 40 in the nation testing what is called Diaspirin Cross-Linked Hemoglobin.

Through filtering and pasteurization, the solution concentrates hemoglobin, the blood component that carries oxygen to the body's tissues, while reducing the risk from other blood-borne infections.

The experimental treatment is designed to increase blood flow and oxygen and stabilize patients who have lost a lot of blood. It will be given in addition to standard treatments, such as transfusions, fluids, medication and surgery.

The hospital said it would do everything possible to get consent from the patient or his or her relatives, but acknowledged that in some cases of extreme injury, that might not be possible before the treatment has to be started.

Richland Memorial's trauma services unit treats about 1,500 patients a year. Hospital officials estimated 20 patients will be eligible for the product during the next 12 months.

Attachment 42

Hospital Liaison Committee *for* Jehovah's Witnesses

Allentown, Pennsylvania

000-000202

SERVING THE LEHIGH VALLEY - NORTHEASTERN PENNSYLVANIA - NORTHWESTERN NEW JERSEY
SHARING RESEARCH ON ALTERNATIVE NON-BLOOD MEDICAL MANAGEMENT

PRESENTATION AG[illegible]

ALLENTOWN, PENNSYLVANIA
HOSPITAL LIAISON COMMITTEE
for
JEHOVAH'S WITNESSES
SERVING THE LEHIGH VALLEY-NORTHEASTERN PENNSYLVANIA
NORTHWESTERN NEW JERSEY

For Emergency and Confidential Use Only

Written Replies to: J. M. Brazil • 3271 Mountain View Dr. • Danielsville, PA 18038-9782

I. Introduction-(2 min)

II. Our Position on Medical Treatment-(3 min)

A. Informed Choice - Not "Right to Die"

III. The Doctor/Patient Relationship-(5 min)

A. Conscience of Doctor/Patient

B. Options for Doctor/Patient

C. Protocol

IV. Acceptable Alternatives to Blood Transfusion (10 min)

A. Nonblood solutions

B. What about blood storage, fractions, serums, autotransfusion?

V. How we Are Set up Internally to Look After Needs of Witnesses

1) Hospital Information Services
2) Hospital Liaison Committee
3) Visitation groups
4) Ongoing education

VI. A Sensitive Matter: Treatment of Children-(7 min)

A. Parental responsibility

B. Legal issues

C. Doctor's options

VII. Conclusion-(1 min)

VIII. Questions and Answer Session-(15 min)

ALLENTOWN, PENNSYLVANIA HOSPITAL LIAISON COMMITTEE *for* JEHOVAH'S WITNESSES

SERVING THE LEHIGH VALLEY-NORTHEASTERN PENNSYLVANIA
NORTHWESTERN NEW JERSEY

For Emergency and Confidential Use Only

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Attachment 18

Second Town Meeting at Schukyll Falls Library

Dr. Sokil is here to be able to answer any questions that you may have about the institutional commitment to the protection of people that are involved in research studies at our institution in particular.

My name is Thom Santora and I am one of the trauma surgeons over at AUH/MCP. Vince Cole is one of my associates in the Department of Anesthesiology. We are coming to you today to discuss an opportunity that we have to help the patients that we see on a daily basis. As a trauma surgeon I am called down to the Emergency Room very frequently, just about every night that I am on call, to try and evaluate and put back together people that have been severely injured. For example, not long ago an individual from this community was walking along the railroad tracks down here and had his walkman on and did not here the train coming and was struck by the train. This fellow came into the Emergency Center, as you can imagine, he lost that battle and was pretty badly injured. When he came in his blood pressure was low and he had evidence of bleeding into his belly cavity. He would have been a candidate for this study. Fortunately for him we were able to get him to the operating room and get him patched up, but that gentleman spent about 3-1/2 weeks in the hospital and required two operations to get that done. We had another child not long ago that was involved in a motor vehicle crash on Roosevelt Parkway. A minor fender bender got out of the car and in fact was truck by another vehicle

and dragged 100 yards down the road. This child was brought in to the Emergency Room with barely a pulse. We were able to get her pulse back and take her to the operating room where she had extensive intra-belly injuries and a badly broken pelvis and despite our best efforts, this 17-year old girl died on Christmas Eve. These are the tragedies that Dr. Cole and I see on a daily basis and this is just a couple of examples of what could be said of 140,000 Americans every year that dies as a result of injuries. It happens to young people, old people, people of all race, religion, creed, you name it. A vast majority of these folks are in the prime of their life and, in fact, trauma is the leading cause of death for persons under the age of 44. So this is a cataclysmic problem and right now when patients come to our Emergency Centers and their blood pressure is low from bleeding 40% of those people die despite our best efforts. 4 in 10 patients despite Dr. Cole filling up the tank and me trying to get control of the bleeding they die. That is unacceptable to us as people who see this on a daily basis and I would hope to think that this is unacceptable to the community as well. That is what we are here to talk about; is the opportunity to change some of those numbers. We were invited to participate in a research study of a blood substitute that has been shown to have promise to improve blood pressure and improve oxygen supply to injured patients. Oxygen is our most important nutrient that keeps ourselves alive and we have been taught through medical school that injured patients have 60 minutes, which is called the Golden Hour, after they are injured by which if we could fix the blood flow to vital organs we have a

fighting chance to get a patient through even severe injuries. The hope is that with this research study we will use this blood substitute in addition to the standard treatment that we use today that is the same in every trauma center across the country, but we want to look at this medicine that will be given shortly after a patient arrives in addition to the standard treatment to see if this medicine can improve the blood supply during that Golden Hour so that we can potentially get more people to survive. Just as I was talking to a man in the back, this medicine is not expected to be the same results as we saw in the 1940's with Penicillin. When Penicillin first came out we gave it and peoples infections were cured. We do not expect that with this medicine. There are going to people that are going to get this medicine and they are going to die anyway because there injuries are too severe but what we are hoping is that it will reduce the number of people that die by 25%. Say instead of 40% mortality in the standard treatment we expect to see about 30% mortality in the patients that get standard treatment and this blood substitute. That may not sound like a whole lot but, in fact, if we talk about 140,000 Americans and we can reduce the mortality from 40% to 30% we may be looking at saving upwards about 35,000 Americans every year and one of those people may be God forbid somebody that is near and dear to our hearts. That is really what we are trying to do is to service the community. We as medical people that see this side of our community activity see this as a huge problem. It is killing our young people. Is this the fixed of the problem that we see on a daily basis, absolutely not. We need to take the guns out of the hands of kids, we need to

take the bottles and the drinking out of the people behind the wheel, that is going to fix those problems but until we do we as people that take care of injured folks need to have better tools to take care of these folks.

Another person:

To explain a little bit more about ??? is that the reason we are here is that this blood substitute product called ??? is a substance that has been produced by a company called Baxter Health Care Corporation. This blood substitute has already gone through some experimental research with animals and has also had some human exposure as well although it has not had the kind of exposure in the patient population that we are trying to familiarize you with. What has happened thus far with this research is that the government has sanctioned us to begin trials with this research. If we can communicate with the community to allow them to participate with a voice and feedback information knowing what we are doing and giving us some feedback as to what they feel and what they think about this process, about the research, about the possibilities of being affected by what we are doing. This blood substitute product again is primary purpose is to carry oxygen to the vital organs so that the cells receive the nutrients from the workup of this blood substitute may perhaps a better chance of surviving the critical period in which the person is literally fighting for their lives. The government has allowed us to use this without having to get consent from the individual because of

the circumstances under which most of these patients come to the hospital. Most often the patient comes to the hospital and may not be accompanied by loved ones or may not be accompanied by someone that is in the position to give consent to us care for the individual and quite obviously the individual themselves are not in the position to give their consents. In the event that someone is with the individual that is in the position to give consent, we would follow the normal protocol that follows in any situation ?????

This being a husband, wife, child, etc. ??? Tape gets lower and I cannot here what he is saying.

Question: ??

Thom: Every case. Right, but the problem we are faced with is that trauma is unpredictable. We could walk out that door and get hit by a car and unfortunately that happens all to frequently and then the patient is brought to the Emergency Room with life threatening situations and there is no one accompanying that patient. However, we will inquire whether or not there is some there, we will look through their pockets to find out who this individual is and try and contact a love one as we do now to let them know what the situation is and under those circumstances ask if they would participate in this research trial.

Question: ??

Thom: At this point in time the federal government in this three year process has put a moratorium essentially on doing research of any kind in the face of emergent circumstances because when people come in either with heart attack, Dr. Sokil's other hat is that he is a heart doctor, and when people come in having a heart attack there are certain things that have been put on hold because that patient really can't give an informed consent because they are too concerned about dying. So in a situation very analogous to the patients that we take care of under these circumstances. So in three years the federal government working with scientists, ethicists, lay people have developed guidelines that just went into effect November 1, 1996 that stipulates that if you have a life threatening situation and you have a study treatment whether that means some medicine, a blood substitute, some kind of operation that has shown more benefit then risk and that there is no other way to do the research trial and that the federal government has looked at the exact plans for the research and have found those to be acceptable and the group that Dr. Sokil heads at the individual hospitals has gone through the same process in looking at the protocol the exact steps that the researcher will do if those two groups are found appropriate then a patient can be enrolled with an exception to informed consent. The additional safeguards for the subjects because the individuals often times won't be able to give consent because they are not thinking clearly because their blood pressure is low is to go out into the community as we are doing now and to try and reach the people that potentially may be subjects for this research, God forbid anyone in this community, but the

point of the matter is trauma is completely unpredictable and if the community is aware of what we are doing and they have the opportunity to come to us, hear more information, voice opinions and concerns and essentially the sense that we get and Dr. Sokil's main purpose here today is to get some feedback from you as a group. If you see this is beneficial and you see the problem as life threatening then we would proceed. Now if the community said I do not see this as a problem meaning that it is okay that 40% of people that come in like this die, I do not see that as realistic, but if that is not perceived as a problem or just for whatever reason don't like the idea of the research or you don't like the idea of having individual patients rights taken away then we are not going to proceed. Let me speak about the rights of the individual. I for one will always seek love ones to tell me what to do and help make decisions. That makes me feel better. I know what I would do for an individual if I had the only say in thing but what I am saying does not matter for the individual patient. That patient is the primary decision maker and, when that patient cannot speak for him or her self, and it is the family that knows that individual best they should be able to speak for them and that is how we do business. However, I also believe that the most sacred ?? is life itself and the way I see this is that 40% of these people that come in that fits this bill are going to die. So they lose that right to life and with this product I might be able to save some of those people. That is the right that I think gives us the right to proceed with this exception for informed consent but we have to do it properly.

Question: ???

Thom: First of all the study is not continuing it is just being started. The way that the federal government and the FDA in particular oversees a drug development it has to show that the drug is first off is safe and it gets to that point only after it has been shown to be effective in laboratory animals. So if the drug is not effective in laboratory animals then there is no reason to test it in humans because why would anybody regardless of how safe it is want to use something that is ineffective. Animal laboratory studies are important because what efficacy it is shown to various treatments are often times equivocal to the human. So that if we were develop a model where animals have bled given this material which has been done it has shown that the animals that received this medication lived whereas the other animals that do not get the medication died. There is a difference between those two groups. So there is demonstrated improvement ?? terms of life in animal studies. So that information is fed through federal government and says that this drug looks promising therefore lets start testing it in humans. The first part of that testing process goes through a ?? base process where the first two phases are to look to see how the drug is handled by the ??? ?? and then once it has been shown you know how the drug gets eliminated from the body and those sorts of issues the next question is, is it safe at increasing doses. Safe in terms of does it cause damage to the lungs, ??? and those tests have been done in humans and the drug is shown to be safe. Now the last phase for federal FDA approval ??? shown in those

patients. Its efficacy has been shown to be basically reducing the amount of blood that was necessary in heart patients undergoing heart bypass surgery. It has not been tested in the population of trauma patients to look to see if it would improve their outcome. That is the study that we are about to undertake. I think that it is going to be beneficial because it does the things during that "Golden Hour" that we need to accomplish and that is to improve blood supply by carrying the oxygen to vital organs so that we have a fighting chance. Could it cause problems? Sure it could as it increases the blood pressure which this medicine does very shortly after giving it the blood pressure goes up so as the blood pressure goes up we may find that the bleeding increases that has not been shown in the case in animals studies but it might be in the human study that is why ?? those results in animals may not be the same in humans.

Question: ???

Thom: High blood pressure, no, there is a couple others that are fairly common ?? one is that ?? discolor the skin in transient meaning that the medicine that lives in the skin for a period of up till five days and ????? eliminate through the body and as such tends to turn the skin a yellow color. You might appear to be jaundice ?? Jaundice will leave you ??? medical doctors ?? usually means that there is a problem with the liver and the patients that have gotten this medication and there skin has turned yellow there liver can actually ???. What has been found is that the medicine

itself is in your skin and with a light shining on it it turns yellow like babies that have high bilirubin levels shortly after their born. It is the same sort of thing. The other common side effect is ????? and some of it ????. Now other side effects that I do not think we will see in our population because our patients are so sick they won't be able to complain. Often times ????
but bloating, gas pains, ???. Again, I don't think that ????
Now the blood pressure effect can be conceived as an adverse side effect ??? where our patients come in with low blood pressure ???? ?????????? blood pressure can rise up to about 35% where it started from. So if someone starts off low and then goes up to normal ????

Question: ??

Thom: Well again that is the possibility if you start off with ???
It is an enhancement. It is just a substitute for blood ???????

Tape is too low to hear!!

Attachment 19

Community Meeting
Pickett Middle School
Thursday, April 17, 1997

Question (female): You said that you use a blood supply from the red cross which is normally discarded after 42 days because if you use that blood after the 42 days there will be adverse affects. So they take it and with a few modifications now it becomes a blood substitute. Do we know if any if there is any adverse effects from the blood substitute? I mean has this been done before? Do we have results somewhere that say this actually helps or doesn't help or have some side effects?

Answer (TAS): Yes. The way this medication, any medication gets approved by the Food and Drug Administration is a very regimented step wise process. First of all, the medication, our blood substitute in this case, is tested in laboratory animals because they want to see if the drug has potential beneficial effects. In study animals this medication in fact does have a better outcome in animals that were bleed to the point where their blood pressure was quite low. They compared this blood substitute to blood and to other standard ways of trying to increase the blood pressure; salt water solutions, albumin, those sorts of things. The animals that received the blood substitute did significantly better than the animals that received the other treatments. So in laboratory animals, there is no doubt that this medication, this blood substitute has benefit at improving survival from bleeding. Now what the FDA then had to see was, is this medicine, this blood substitute, safe? In other words, if you give it to people will they have problems.

some gas pains after you administer the medicine that are transient. But our patient population will be so sick from their bleeding, they will have a breathing tube in place, be under anesthesia, most likely they won't have these complaints or those problems. So those are the adverse affects that are seen.

Question (same female): Since patients normally have high blood pressure or kidney problems will they be candidates for this? How would you not know that?

Answer (TAS): Well, no we don't know that. The only thing we'll know about these patients most of the time is that they've been injured and when they come to us they have a low blood pressure and evidence of bleeding and, in fact, the person that comes that has high blood pressure under normal circumstances that now presents with a very low blood pressure are at even higher risk of having a bad outcome because their organs, like their kidney, needs to see a higher blood pressure to function. Their organs have become used to seeing a higher blood pressure. So it is crucial especially in those people to get the blood pressure up as fast as you can.

VC: In those situations where people come in as trauma victims preexisting diseases, be it high blood pressure, diabetes, or whatever, all of that takes a back seat to the immediate needs of trauma patients, so we're not worried about treating somebody's high blood pressure. At that point in time your priority is trying to provide cellular nutrients, primarily oxygen, by getting

as much material that carries those products into the body faster than it is coming out of the body.

Question (female): Can you tell us how long this research study on this medicine, I'm calling it now, has been and if we can find out what other ingredients are in this medicine. I mean we first started talking about a blood substitute and now we are calling it an actual medicine. So I want to know some substance other than, you know the hemoglobin being re-oxygenated is what I thought I heard but, I mean medicines are made up of more stuff.

Answer (VC): We sometimes interchangeably call it a blood substitute or a medicine and its because its a little bit of both. What it actually is what Dr. Santora already said. Everyone's blood has hemoglobin. Hemoglobin is one part of the red blood cell but it is the prime part that is responsible for carrying the oxygen to the tissue. Every time you breath in oxygen gets into the lungs and into the blood system then the red blood cells carry it to the different tissues attached to hemoglobin. So what they've done is stripped away the red blood cell and taken the hemoglobin, packaged it so that we can get hemoglobin alone without the other components of blood; what it does is it essentially just buys us time. It doesn't eliminate the fact that we still use blood in conjunction with all the other things. We haven't made that clear, and I want to make that clear, this is just another tool in what we'll be using in trying to save someone's live during the resuscitation process. We will still give blood. You will still get red blood cells, and platelets, and fresh frozen plasma, and saline salt water, and putting in a breathing tube, and

getting you to the operating room. Everything continues, in the same manner. The only thing that we plan to do differently in the study is that when you come into the emergency center and you fit the criteria meaning, your blood pressure is lower than 90, your pulse rate is higher than 120, or your heart rate is in what we call a preterminal rhythm, that it appears that if we don't correct things soon the heart is going to stop functioning properly, then you will be selected to either receive the blood substitute or receive saline. Over time we'll look to see if there is a difference in the two groups of people. If the people that got the blood substitute do better than the people that got the saline. But the substance itself is a blood substitute, not a drug. It's not so important what we call it as long as we understand what it is.

Question (female): I understand it is not important what we call it, I'm interested in what it is. What is in it. What is made of. That's my interest.

Answer (TAS): Yes. It's just hemoglobin. That's all it is.

Response (same female): Do you have any written material that we can have.

Answer (TAS): Sure we do. This blood substitute has been studied for 10 years. Okay? It has been used in patients over the last four years and again it's been going through that step wise process of being evaluated. The way drugs are studied is again, you try to make certain that the drug is safe. Okay? This is one of the first trials to see if this medicine or blood

substitute has made an improvement in outcome. We have demonstrated it has been used in over 350 people to show that it is safe.

Response (same female): Do you know where that was done at?

Answer (TAS): It has been all over - in Chicago, in Boston, in Hartfield.

Question: If this drug has already been given to patients then why do you need to do this study, and how many of those people are now dead?

Answer (TAS): All of them are still alive. The study drug, in this case is a blood substitute, still needs more investigation. The phase that all medicines go through to be approved by the food and drug administration is that they go through this phase to figure our if they are safe first. Okay? And then they go through another phase to see if they have a beneficial outcome difference. In other words if I give, God forbid, you this medicine and I don't give it to the gentleman sitting across the hall and you have the same degree of injury in bleeding will you have a better chance of living than will he? When everything else is equal, in other words, we are going to do the same operations, the same amount of fluid and blood and everything else that we normally do today, the only difference is that we are going to give some people shortly after they arrive to the hospital a small volume of this blood substitute in addition to all of their standard treatment and the other group is going to get an equal volume of salt water and all the

standard stuff that we do.

Question: How will you know if the blood substitute is causing problems?

Answer (TAS): Part of the care that we provide to people after injuries includes tests or various laboratory studies that allow us to look at the damage to liver or damage to muscle or damage to the kidney and that's part of the process of caring for the patient, and in particular when you have a research trial. We want to make certain that there is not any adverse reactions in this population of patients, so we will be looking at those things. One of the things that the federal government wants us to do, if we are going to use this exception to informed consent, is to report to a special panel, a safety panel of people that are not involved with the study at all that are going to see the data, the results of the study as people go through the study and if they find that there is an unexpected high adverse affect rate they're going to shut the study down because they don't want to take that chance that we might have an unexpected outcome that could be negative in this patient population. On the same token, when we forward that information to the safety board if it is overwhelmingly positive, then they will stop the study and say you don't need to look and deprive half of the study population of not getting this medicine, because the people that have received it so far have done so much better than the people that haven't is that this drug is obviously good under these circumstances and then the FDA will say we approve this drug, use it on everybody in this circumstance.

Question (male): Who do you expect will be the main people involved in this study?

Answer (TAS): It's to help anybody who comes into our emergency room that has low blood pressure from bleeding. It doesn't matter what race, creed, or age.

Response: Well I've been to MCP's ER and I saw black patients not getting the same treatment as other patients.

Answer (TAS): Well I'm telling you that, I'm standing here today and I will refute that with you as long as you want to have that refuted.

V.C.: I support what Dr. Santora says, but I think we are getting away from the main issue.

Response: Well I think how we're treated is the issue.

V.C. - Let me say this is one of the reasons that I have a personal interest in this study. Do you know what the number one cause of death in young black men between the ages of 18 and 35 is.

Response: Yes, trauma. Now let me ask you who else is in this study?

V.C. - This trial includes 35 centers across the county. Some of the hospitals that have already started the trial are Allentown Hospital, Washington Hospital. Hospitals that are inner city as well as hospitals that are in the suburbs.

Question: Do you have data in writing

V.C. - Everything that we are saying here is documented in prior research articles. Everything we're saying here is documented.

Response: How come we haven't heard about any of the other studies?

TAS - The allentown study has been in the Inquirer. It was in the Inquirer about a month ago.

Question: Could I go to your hospital and get any of this information. I would really like to have it so I can read it before the study starts.

TAS - Sure. We have some background information.

Question (female): I was surprised that you didn't bring something for people to see. You are taking community opinion about this. How and when will you determine what the community decided. From this group of folks here tonight? What?

Answer (TAS): You are a representative of our community.

Question (same female): Is this a one time shot presentation?

Answer (TAS): We have made ourselves available to the community that we serve. This area is only one part. There has been three separate meetings that we discussed this research trial at and we have had a radio show. We have had a newspaper article and the issue of reaching out to the community, I will tell you is a new phenomenon. Okay?

Question (female): So how when will you make your determination yes or no? I need to know that. Without anything I can look at in terms of these 350 people, sure they may be alive but what is the quality of their life. People want to live, but they want to have a good quality of life. So for me, I need to know that because there is a lot of things vivid in my mind regarding African Americans and medical care and research and all of that and it has not been our favor. Frankly, I feel. I need to see something. For me to sit hear and listen to you tonight and say oh this wonderful to save people's lives I wouldn't want that for my family or anyone else's family in this community that I work in and serve in and live in.

Question (female): Now you say this is a blood substitute?

Answer (TAS): This is a blood substitute. Yes.

Question (female): From what I understand the reason why you are out here is to get our response. So if somebody comes into the hospital as a trauma and then gets it will be because of our approval?

Answer (TAS): That is somewhat what we want to do. We certainly want the increased awareness. This is a multi-fold process. We are out here. If we heard absolutely negative things from you saying we wouldn't want to be involved in any kind of research I don't care what if, ands, or butts about it, we wouldn't want to be involved. We would take that back and we would discuss that, but the important issue if nothing else happens is the education that is going to occur tonight. I don't know how many of you have thought about just how grave this problem is for our community.

Question (female): From what I understand this particular medicine ??? is not going to do ?? so

Can't hear.

Question: One you said something about they wanted to test it on people to see whether or not there is any adverse affect, I thought the procedure was to do research on animals to see what side effects then if there weren't then you'd test it on people.

TAS: That's been done.

VC: Animals trials have already been done as well.

Question: Isn't this a trial area here.

VC: This is just a different patient population. Human trials already been done on stroke victims, and patients undergoing cardiac bypass surgery. This is now trials on people who are severely traumatized with bleeding injuries.

Question: So that 350 is that the total number of people in the research or was that 350 out of another number.

VC: That's 350 people that have already received the blood substitute. This trial that were undergoing will hopefully comprise a total of 850 across the 35 centers in the country that are participating in evaluating this substitute on trauma victims, so this is a different patient population.

Question: How long are you going to follow these 350 people? How long are you going to follow them to see if there are any side effects.

Answer (TAS): The blood substitute lasts in the body about 48 hours. Okay, the various trials have looked at them for months but once the medicine is out of the body it doesn't have any

lasting effects. All the effects of this blood substitute are transient in nature. In other words, they come very rapidly and then they go away as the medication is eliminated from the body.

Question: You mentioned something about the panel. The panel is only going to be made up of medical professionals or are you going to allow the community to partake on the board.

Answer (TAS): Well there is actually a number of panels and Ms. Denega and Ms. Schieffield sit on our what we call the Committee for the Protection of Human Subjects. Any hospital that does research has to have a panel of people that are comprised of investigators, legal people, representatives from the community that will review each and every study protocol. In other words, the investigator, our plan to look at this study medicine has been reviewed by this panel of people at our hospital. In addition, this plan has been reviewed by the federal government and both of those panels in every one of the 35 centers that will enroll patients in this trials will have a similar panel at their hospital and will have to review the plans and demonstrate to themselves that this medicine or blood substitute is more safe than it is risky and more importantly, that it has the potential to be beneficial to the people in this circumstance.

Question: What country are the patients from that already received the blood substitute?

Answer (TAS): United States

Question: Does the hospital purchase the drug or does the drug company donate it.

Answer (TAS): The drug company provides the blood substitute.

Question: So they are giving you the drug?

Answer (TAS): That's right.

Question: What drug company is that?

Answer (TAS): Baxter Healthcare

Question: I just have a question - this will only be used in the trauma center? Correct? Someone going there for routine surgery that might need blood on hand during surgery will not have to decide on this substitute.

Answer (TAS): At this point, No. Only people who come in severely injured.

Question: Okay, now who decides who gets it and who doesn't? I mean if your researching you need something to compare it to. All things being equal if two people come in with multiple trauma or whatever, somebody gets saline and somebody gets the blood substitute - who makes

that call?

Answer (TAS): There will be a box or a shelf that will have a series of sequentially numbered envelopes and as soon as the patient comes in an they have injury with low blood pressure and evidence of bleeding then that patient regardless of their color, regardless of their gender, regardless of their age, will be enrolled in this trial. And what that enrollment will entail is that the individual will go to that drawer and pull out the next envelope what ever is on that selection will be the choice made for that patient.

Question: When they come in they may be coherent, but they may not been to one of these neighborhood meetings, but they don't know they are getting a substitute. When you say you need blood they may give their consent without necessarily knowing that they're getting a blood substitute. So even you know with the exception to informed consent and informed consent to be very close and even if someone comes in knowledgeable about this and want this and they get an envelop that says saline. They have to get saline?

Answer (TAS): That's correct.

Question: How do you spell your name?

Answer (TAS): S.A.N.T.O.R.A.

Question: Out of all the people that has been exposed to this study so far do you know the racial breakdown?

Answer (TAS): No I don't.

Question: At all?

Answer (TAS): No

Question: And you said that this information in terms of the study is available? Can you tell me how I can obtain that information?

Answer (TAS): The study that we are proposing to you today? I can send it to you.

Question: What hospital do you work for?

Answer (TAS): Allegheny, MCP.

Question: We need to see things. For me, I need to see things and I know a lot of these people here, members of the team, and we need to see things because if you are going to treat someone who is unconscious based on our decisions whether you want to go with this or not, well, that's

a responsibility. My other interest is this drug company who is making this drug and giving it to you, why? What is their interest?

Answer (TAS): The interest is obviously companies want to develop medicines that ultimately if they prove beneficial they can make money from. I mean that's reality.

VC: This study isn't any much different than every drug that has been developed - that goes to developmental trials. Where it goes to different phases of research until that drug proves itself to be beneficial regarding health care.

Response (female): But they never come into the community and say do you want this or not?

VC: No. It is because this particular protocol has the stipulation of community disclosure and that is why we are here. The point is if the FDA did not say that with this protocol you need community disclosure then we would be doing it the way most research is done. That is you come to the hospital and you are asked if you would like to participate in a trial called this particular drug. Sometimes trials are done in fact, one gentlemen asked about what country. In fact, some drug companies, because it is easier to do human studies over seas in countries that have less stringent regulations. But at the same time, when people find out about some drugs that are being used in other countries and not being used here, people may get upset because that drug is not available. There are complaints that the FDA drags its feet and takes

too long to approve a drug and people may be dying from lack of receiving this drug. So the FDA sometimes gets stuck between a rock and a hard place. Sometimes they say we too slow with approving drugs and then sometime people say well it needs more research and we should take longer to study. What we are trying to say is - we're not trying to say that this drug is on the level of penicillin or anything that is going to revolutionize medicine, every victim that come in the hospital resulting from trauma life is going to be saved, that focus is not here. What we expect and what we hope to project is that we may be able to improve our care to these people. 40% of people who come in with sever trauma die. We hope to try to decrease from 40% to 30%, which means a 25% decrease in the amount of people that die. And again, this is just one more tool at an attempt to try and save people's lives. Again we don't propose this is going to be again a miracle drug. This is just one attempt to try and identify if in fact this drug will be helpful. We came here very expectant that there would be a lot of sensitivity to issues that this protocol is going to be something that maybe tested on blacks or indigent population alone, people who don't have as much of a voice to say aye or nay. This protocol is not concentrated on inner-city or suburbs and it is hopefully evenly distributed.

Doreen D: I think the important thing to do is to let you know that this type of research would not be done. The government thought that this type of research was so important that they created an exception. This is a just a new exception to the law that would allow researchers to come into the community, talk with the community and say will you give exception to the informed consent so we can try this important research. Again, nothing with age, sex, women have been told that they been discriminated against in research. It has nothing to do with it.

The government thought that the trauma research was so important that they wanted to carry out trauma research so that they would create an exception to the law.

Question: What I can see. Let me ask you this. How long ago has it been the 350 people in the study. Has been it long enough to see any long term side effects? Has it been a year? Two years? A month?

Answer (TAS): It has been over the last four years that those people have been

Question: Were they all given it at one time or a few over the four years?

Answer (TAS): past the four years.

Question (can't hear):

Answer (TAS): I think what I am hearing is a lot of skepticism and we expected that and you have every right to be skeptical. But I'll tell you if we or others that follow us can't do these types of research because people have skepticism because of track records.

Response: You don't think that we have reason to be skeptic?

TAS - Absolutely. There is no doubt about that. But the reality of life and we know this is that people in our community are dying left and right.

Response: I understand that.

TAS: And if the skepticism that you have will keep you from having an open mind about potentially beneficial therapies then unfortunately that's how it's going to be cause we're not going to have the tools to be able to change the outcome.

Response: But see I don't want to be one who you come back to latter on after 300 or 400 people have come up with something with really weird or their children have birth defects and say you are people in the community that wanted this. It just strikes me really odd, and this is my own personal opinion that the decision lies with the community - you know that's my own feelings about it and I need to express that. Yeah because I don't want to have that responsibility, whether its my child or not. For someone who couldn't make that decision on their own for us to say, you know, for me to say it's fine go ahead and do it and then later on, you know, their kids are messed up or whatever. I wouldn't want that, that's why people want to live, but people want to live with a good quality of life and until I see something from someone who has had this.

Answer (TAS): How would they ever get that Ma'am?

Response: I don't know, but that would be ridiculous for me not being knowledgeable of this and say yeah.

V.C.: That probably isn't - you know I don't know how realistic that is. A person that comes in trauma may have a hundred things done to them. That person can't say because of the blood substitute I am now this or I am now that. What you do is you try as best you can to identify if there is a significant indicator that says that people have similar injuries yet this one appeared to do better overall then this person.

Response: Well, you give blood to patients that are approved by the FDA that come in and have to have an operation or something and they're in a trauma - you treat them. You treat them anyway. You give them so many cc's of this and that - these are things that are already approved by the FDA and you use those tools and you treat the patient. Why is it now that you can't do the same thing.

Answer (TAS): Despite that 40% of people die.

V.C.: Stop here. Just because you save some people. You say oh well, we're saving 60% of people so we don't need to do anything further?

Response: That's not what I am saying. You treat people now with drugs that you didn't get

the community's say. It's approved by the FDA and you treat people with these drugs, why not use the same procedure with this.

Answer (TAS): Because as a community you need to know what we're doing.

Response: Yeah, we agree with that.

Question: right of a patient. At that point you don't have any rights.

V.C.: You haven't given up your rights.

Response: It is to me, and I'm afraid to do that. It's just a door that is opening because if the federal government is saying now that you can introduce a drug and you don't have to get the patient's consent to use it, that is giving up the patient's rights. Just because of his condition and what ever else is going on. You know, once you start this you will open this pandora's box. How far is this going to go. What's going to come up next year. Well, we can do education if the doctor feels it is necessary. To me, that worries me, with the clinical studies being able to just do it without patient's permission.

Answer (TAS): You have every right to be skeptical about that first off. The issue really revolves around how big you perceive the problem that are faced by this particular patients.

These people are dying. Okay? And we are able to save 60% of them and that sounds like a big number and in fact it's not bad, but you something we have been able to do that for 50 years. We haven't been able to

Question: This isn't the cure all either, I don't believe.

Answer (TAS): And we don't think so either. There are people that come into our hospital and despite anything they need a miracle and this is not a miracle, but we need to have better tools, there is no doubt about that and the issue is that the only way that we can test tools is to be able to do them in the people that are fighting for their lives and under those set of circumstances, the patient is always going to have this quandary of you know, are they really able to understand what we are talking about to give informed consent, because it is tough to do informed consent.

Question: But there are patients with like blood disease, like leukemia.

Answer (TAS): Yes Ma'am. There is no doubt about that.

Question: Why are there not any clinical studies on those patients.

Answer (TAS): That's not what we are asking of this medication. We know that the drug carries oxygen. We know those things.

Question: Those things will benefit those patients as well?

TAS: What do you mean? What things?

Response: The blood drop. The blood levels drop and they need the oxygen supply to their organs as well. If that blood works with the trauma patient would it also work with the patient that had leukemia.

V.C.: Those are different, very different diseases. People who have leukemia have problems with the production of white cells by cancer tissue. That and oxygen supply are two different things. Again, I just wanted to clarify that. The blood does many things. The blood carries oxygen, carries nutrients, carries proteins, it carriers clotting factors. This is just one part of what blood does, carry oxygen.

Question: I am speaking from personal experience. My sister is a patient at Marriah Farm Hospital in North Carolina. Her first amputation wasn't very successful. The second amputation she did receive blood substitution. I don't believe that she is not living today because of the blood substitution, however, she did survive six months after blood substitute. My family however, does not feel that way. They feel very negatively about the blood substitute.

V.C.: I doubt it was this blood substitute.

Question: Well how many are there?

V.C.: When you say blood substitute. There may be many things that lay people may refer to as a blood substitute that may not necessarily be.

Response: I'm quoting exactly what the nurse said to me when I called the hospital to see how my sister was doing.

Answer (TAS): Was your sister a Jehovah Witness.

Response: No, no she's not.

TAS: The reason that I say that is that Jehovah Witnesses have a religious reasons, but they will take a blood substitute, but not this blood substitute because this particular blood substitute is made from blood cells. I'm just trying to clarify this. Again, this must be very frustrating to you because this is complicated stuff and some of the things that we say may seem that it is conflicting because

Question: Does this drug have a name?

TAS: Yes. This stuff is called, Diaspirin Cross-Linked Hemoglobin.

Question: Spell it please.

Answer (TAS): The commercial name is hematest. H.E.M.A.T.E.S.T. Diaspirin Cross-Linked Hemoglobin. D.I.A.S.P.I.R.I.N. Cross-Linked H.E.M.O.G.L.O.B.I.N. So what we are before you today is to talk about the blood substitute that is made from human red blood cells that has human hemoglobin and the process of making this blood substitute is called Cross-Linking and what happens is this blood is obtained from the blood bank because it sat on a shelf longer than 42 days. The drug company prepares this by breaking the coating of the red cell and then cross-linking the hemoglobin so that it can carry oxygen.

Question: Cross-linking it with oxygen?

Answer (TAS): Cross-linking so that it stays together. Hemoglobin is made of four parts and it cross links the two strands so that they stay together.

Question: So you use something to cross-link it?

Answer (TAS): Diaspirin.

Response: Okay, that's why I was asking what was in it. I knew it wasn't just hemoglobin.

Answer (TAS): But it's all hemoglobin. But the important thing - this is very important. When the drug company makes this it takes the blood that's been screened for HIV and all the viruses in the process of donation through the red cross, it takes those precautions and to that it adds heating this hemoglobin and filtering it and pasteurizing it which makes this product much more unlikely to transmit viruses which are inactivated by heating and pasteurization. So in essence, this blood substitute has less change of transmitting AIDS or any other virus than blood banked blood.

Question (male): I'm saying that all the research and studies you know no racial breakdown at all?

Answer (TAS): I have to say that I don't know. I really don't know. I don't know the breakdown.

Question: But you can get that breakdown right?

Answer (TAS): I don't know.

Question: Do you have any other plans for community meetings like this? And will you have

a scheduled time line for implementation?

Answer (TAS): We would like to see this be the last meting that we have. We've had two other meetings in area communities and pardon me.

Question: Where were the other meetings?

Answer: At Deveraux Church in North Philadelphia and in East Falls.

Question: How will we find out the results of the study?

Answer (TAS): The thing that we can do is to send a letter to each of you who sign into these meetings and to key individuals that we've identified in the community to tell them about these meetings at the completion of the study we will tell you when we will have a meeting to discuss the outcome of the study. That's what we owe to the community.

Question: Can we ask if it was favorable or non-favorable at those other two community meetings?

Question: It was not during the amputation that the blood substitute was given. She wa four days post-operation and was given this. She had very low blood pressure and she was dying and

this is when they gave her the blood substitute. I just wanted to clear that it was not given to her in the appearing room during surgery.

Answer (TAS): Was that as part of the research program, Ma'am.

Response: I did not find out about the blood substitute until I called to check on my sister and I was told at that time that they almost lost her and they had to give her a blood substitute and that was what concerned me. I was basically the contact person and I don't recall anyone trying to reach me.

V.C.: Under those circumstances, if it was this, if a person they can identify as someone who can give consent, they would not do anything. They would not enroll anyone who has the ability to give consent without obtaining that permission. The only time with this study that we would do that is if there was no one available. If there is a contact, someone was in the emergency room, if there was a name on the chart or anything identifying as someone who can give consent, that person would absolutely have to be notified and their consent would have to be given.

Response: I am going to request the hospital report. Because I know for a fact it was told to me that it was a blood substitute and they did have a contact person.

Answer (TAS): We don't even know if that situation was the same blood substitute.

Response: I did also mention that it may not have been the same blood substitute. How many are there?

Question: How many are you using?

Answer (TAS): There has been a number of blood substitutes that have tried to be developed because the blood bank business realizes that there is a lot of blood that sits on the shelf that doesn't get uses. Because with blood you can only give blood to someone who has the exact blood match to your type of blood and these blood substitutes, one of the beneficial aspects of these blood substitutes is by stripping off the coating that has all of the markings for their blood type you can give this hemoglobin to anyone. You don't have to give a blood type. So that's one of the advantages of this blood substitute.

Answer (TAS):

Answer: That's

Tape ended.

Attachment 20

000-000145

Margeret M. McGoldrick
President and Chief Executive Officer

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April 1997

Dear Key Community Member:

Allegheny University Hospitals, MCP has been chosen to participate in a research study for a new blood substitute for trauma patients. This research could potentially prevent the harmful effects of blood loss in severely injured patients. Because of the unique aspects of this research, we are hosting community meetings to discuss this research and its impact on the community.

When researching new medical treatments, the first step is ensuring patients understand the study and voluntarily consent to participate. However, emergency medical situations where life and/or limb is in jeopardy present a unique challenge. Due to the severity of the injuries, it is usually not possible to obtain informed consent from a trauma patient or an immediate family member before the patient requires treatment. Thus, it is difficult to develop new and better therapies for trauma care. For that reason, this study is to be performed with an "exception to informed consent," meaning that in most cases written approval will not be obtained from the patient prior to treatment.

These meetings are being held to inform and gain feedback from the community about this potentially life-saving treatment. You are invited to join Drs. Thomas Santora and Vincent Cowell, the Allegheny MCP physicians conducting the research study, who will:

- explain the nature of the study;
- outline the risks and benefits of the study;
- discuss the concept of exception to informed consent;
- present patient and community safeguards; and
- answer questions.

The meetings have been scheduled for:

Friday, April 11, at 7 p.m.	Wednesday, April 16, at 7 p.m.	Thursday, April 17, at 7 p.m.
Devereaux United Methodist Church	Falls of Schuylkill Library	C.E. Pickett Middle School
26th & Allegheny Avenue	Warden Drive & Midvale Avenue	Wayne & Chelten Avenue

I hope you (or one of your representatives) can attend one of these meetings and give your valuable input. Research concerning severely injured trauma patients could one day save your life or the life of someone you love.

For more information, please call 1-800-PRO-HEALTH℠.

Sincerely,

Meg McGoldrick

Meg McGoldrick
President and CEO, Allegheny University Hospitals, MCP

Attachment 21

Published in The
Valley Item
April 17, 1997

Also in:
"King of Prussia Post"
April 10, 1997

Similar article in "The Falcon" 4/18/97

New blood substitute could save more lives

By C.L. Chase
Staff Writer

Everybody is at risk, one time or another, of losing copious amounts of blood in vehicle crashes, shotgun wounds, stabbings and falls from heights, among other accidents.

Approximately 140,000 Americans die annually because of bleeding from accidents, according to Dr. Thomas Santora of Allegheny University Hospital, formerly the Medical College of Pennsylvania, in Philadelphia.

Santora said in an interview that a new blood substitute, HemaTest, will undergo evaluation through research that he and a colleague, Dr. Vincent D. Cowell, are spearheading at the hospital, scheduled to begin May 1. He added that 35 hospitals around the country are also planning to engage in this research.

One of their goals, Santora said, is to help reduce the annual mortality rate, because of bleeding, by approximately 30,000 people.

Another goal is to determine if combining infusion of large amounts of salt solutions (given intravenously), conventional blood transfusions, and control of bleeding during surgery – all conventional treatments – with HemaTest will enhance results.

An ultimate goal is to use HemaTest in severe accidents in the suburbs or elsewhere when victims are airlifted to trauma centers in Philadelphia. Trauma surgeons and emergency room physicians refer to the "golden hour," Santora said, explaining that doctors have about 60 minutes after arrival of a victim to improve the blood supply and control injury in an injured person. "Time is of the essence," he said.

Santora went on to say that Allegheny is in the "last phase" of the federal Food and Drug Administration approval program. HemaTest, produced by Baxter Healthcare of Illinois, has been used over the last four years on patients in hospitals throughout the country to demonstrate safety. Results were good, he said. Other Philadelphia hospitals are in the planning stage and, according to Santora, chemical compound known as Flousol was developed and used for a number of years. It consisted of a protein similar to hemoglobin – Santora described it as a fluorocarbon – that carried oxygen into the bloodstream.

The new medication is actual hemoglobin, Santora said, that has been extracted from donated blood that has been screened for viral contamination. Donated blood, even if kept refrigerated, has a shelf life of 42 days. "After that," he said, "it is no longer usable as a blood transfusion product."

Santora said that people who qualify for the study must be older than 18; not pregnant if female; or with low blood pressure.

He emphasized that his work, and that of his colleague, Dr. Cowell, are in a research stage. "We're trying to educate the public about the seriousness of severely injured people. The product has shown to be safe. Now we have to show its effectiveness."

Santora also stressed that use of this new medication would, insofar as possible, be used on "informed consent" by the patient. If the patient is unable to give such consent because of his or her condition, a relative may be brought into the picture, if that is possible.

If all else fails, he said the federal government has made provision for investigators to provide treatment in life-threatening situations without informed consent.

Four-year studies in other hospitals have shown three types of adverse reactions, Santora said. They include an above-normal increase in blood pressure; the skin may show a yellow discoloration, which he said is temporary and goes away within five days, and does not affect the liver; and a patient's urine can temporarily turn red but usually clears up in about 48 hours. Other less common side-effects are an elevation of an enzyme in the pancreas, a transient occurrence that lasts for two to five days; and abdominal gas pains, also transient, that last for two to five days.

Anyone interested in this research program can obtain

Attachment 22

...Page 10 | East Of Germantown Ave., 6/16- 6/20 | See Calendar, Pages 14, 15, 17

Germantown Courier 47

Serving the Germantown community since 1936

Questions, distrust at forum on blood substitute

By JUDY HARTHEIMER
Correspondent

Doctors Thomas Santora and Vincent Cowell, both physicians at Allegheny Medical Center East Falls, came to a Germantown community meeting last Thursday to explain the hospital's participation in a drug approval study.

They were greeted with plenty of hard questions and distrust from the audience last Thursday evening at Pickett Middle School. The meeting was chaired by local activist Supreme Dow, head of the Northwest Leadership Training Academy.

Allegheny East Falls has been approved by the Federal Drug Administration as a testing site for a new blood product called DLCBh (Diaspirin Crosslinked Hemoglobin), which is created from some of the byproducts of expired red blood cells, according to the doctors. The hope, they said, is that DLCBh can be proven effective in helping to save trauma patients who are bleeding so severely that they are in danger of dying.

But most of the approximately 50 area residents who attended the meeting saw it differently. The hospital, they said, was trying to use the mostly African American community it serves as guinea pigs for a product that might not be safe, and the company that produced the new DLCBh stood to make immense profits at the expense of the community.

Compounding the widespread distrust was the fact that the Allegheny study would be the first in the nation to use a change in federal regulations issued last year that allows "exception to informed consent," which means that in life-threatening situations hospitals participating in an approved study can administer experimental drugs to patients who are not capable of giving consent.

The informed consent issue alone was enough to draw fire from community activist Sheila Laney, head of the Block Captains Association of Southwest Germantown. Laney said she was totally opposed to the use of experimental drugs, even in cases where physicians hoped to save lives, on patients who were unable to give their consent. "I have a big concern that you will be giving people experimental products that have not been tested," said Laney.

The new regulations were issued by the U.S. Food and Drug Administration in September of last year. The FDA release outlining change said, "The exception would apply to a limited class of research activities involving human subjects who are in need of emergency medical intervention, but who cannot give informed consent because of their life-threatening medical condition. The FDA is taking this action in response to growing concerns that current rules are making high-quality acute care research difficult or impossible to carry out at a time when the need for such research is increasingly recognized."

Laney and many others at the meeting also questioned the proven safety of the new blood product. "Exactly how many trauma patients have been given this product for you to say that it's safe?" she asked the doctors.

They replied that DLCBh had been tested for ten years on animal subjects, and for the past four years on humans. The study at Allegheny East Falls will be replicated at other hospitals across the country, and is the last step before FDA approval to market the blood product. The compound helps trauma victims, said the doctors, because it is a carrier of oxygen, and can help sustain the function of vital body organs that are in danger of failing because of massive blood loss.

Under the rules of the study, they said, all patients would be given the current standard treatment, and some would be given the DLCBh in addition.

The doctors acknowledged that many subjects in the study might very well be members of the community around the hospital, including victims of violence. "Until we get violence under control we are going to see people come into our trauma center and die in spite of our best interest," said Santora. "Primarily, young people are dying because the technology isn't good enough."

The doctors' statements of good intentions weren't enough to quell the distrust of audience members who said the African American community had been victimized too often by institutions that claimed to have its best interests at heart.

"It seems that the black community doesn't trust any studies," said audience member Vincent Muhammad. "We need to develop our own means of investigating," he said. He also questioned whether figures on the racial background of the people used in the study would be available.

Others in the audience questioned the way the hospital approached the community. "Why didn't you come to the community before you applied for the study?" asked Gerald Calliman, representing Concerned Neighbors of Greater Germantown.

There is no firm date for the start of the study, although it has received clearance from the FDA. Santora said that enough direct opposition from the community could block the hospital's participation.

Attachment 23

INNERVIEW

ALLEGHENY UNIVERSITY HOSPITALS
MCP

Allegheny University Hospitals Begins Development on Program for Digestive Health

To improve patients' digestive health through education and to make cutting-edge technological advances in surgery and medicine readily available to patients who suffer from diseases of the digestive system, Allegheny University Hospitals is currently developing a new Program for Digestive Health.

The Program will enhance current therapeutic and diagnostic endoscopic procedures used for diagnosing diseases of the digestive system, and build upon established strengths within the hospital system in the areas of partial hepatic resection surgery and colorectal surgery, as well as the evaluation and treatment of patients who suffer from pancreatic diseases, inflammatory bowel disease and gastro-esophageal reflux disease (GERD).

The Program will integrate interdisciplinary efforts in medicine and surgery, with the key goal to deliver digestive health services throughout communities in the Delaware Valley. The efforts in medicine will be headed by James C. Reynolds, M.D., Professor of Medicine and Chief of the Division of Gastroenterology and Hepatology at Allegheny University of the Health Sciences. Joel Roslyn, M.D., Professor and Chair, Department of Surgery, will lead the efforts of surgeons from a number of surgical subspecialties in the Program.

The Program will have several practice locations, including sites at Allegheny University Hospitals, Hahnemann, Allegheny University Hospitals, MCP and St. Christopher's Hospital for Children. Each of the hospital sites will provide leading-edge treatments using advanced surgical and medical technology. Nationally and interna-

continued on page 3

ood Substitute Holds Promise for Trauma Victims with Severe Blood Loss

Every year, more than 140,000 Americans die from injury, many of them from severe blood loss that can result from car accidents, gunshot wounds or other trauma. In fact, of those patients who suffer extensive blood loss, 40 percent die despite state-of-the-art trauma care.

Now, a promising new treatment – a new blood substitute called Diaspirin Cross-linked Hemoglobin (DCLHb) – is about to be made available as part of a research study at Allegheny MCP's Trauma Center. DCLHb potentially could prevent the harmful effects of blood loss in severely injured patients. Simply put, this study could save lives.

When a patient loses a significant amount of blood, blood pressure drops, the body's organs don't receive enough oxygen, and shock can set in. When introduced into the circulatory system, DCLHb counters the effects of shock in two ways – it works to raise blood pressure and to carry oxygen to vital organs. It could reduce the need for blood transfusions, and requires no blood type matching process.

In animal studies, this treatment has improved blood flow to vital organs. Over the last four years, DCLHb has been studied. It has been fully reviewed and cleared by the U.S. Food and Drug Administration (FDA) and has received favorable review by our hospital review board and numerous regulatory agencies around the world.

This new investigative treatment will be made available only to the most severely injured trauma patients, including males or non-pregnant females older than 18 who present in shock conditions despite prehospital treatment, and who have evidence of hemorrhage. Immediately following hospital arrival, emergency medicine physicians will assess the patient for entry criteria. Those

continued on page 4

Blood Substitute Holds Promise for Trauma Victims with Severe Blood Loss

continued from cover

patients meeting the entry criteria will receive 500 - 1000 cc (approximately the volume of two to four soda cans) of DCLHb or equal volumes of salt solution placebo within 60 minutes of arrival in addition to all standard interventions (salt solution, blood transfusion, operation or a combination of all). By the design of the study, the physicians will not know at the time of randomization whether a patient will receive DCLHb or the placebo solution. All patients will be followed closely for 28 days after treatment.

When researching new medical treatments in emergency situations such as this, ensuring that patients understand the study and voluntarily give consent – normally required in any clinical trial – presents a unique challenge. Due to the severity of the injuries, it is usually not possible to obtain informed consent from the injured patient and frequently family members are not immediately available before the patient requires treatment. However, excluding patients who cannot give consent under these life-threatening conditions would make it difficult to develop new and better therapies for trauma care. For this reason, this study is to be performed under the new approved FDA guidelines for the "exception to informed consent," meaning that treatment can still be administered in these cases where it is impossible to obtain written approval. Since the patient cannot give consent at the time of the injury, the FDA guidelines stipulate that the community from which the patients are expected to come will be informed of the proposed research project.

Allegheny MCP is taking steps to make the community at large aware of this study and to answer any questions or concerns. An internal review board is overseeing the patient safeguards and community education programs that address the needs and concerns of the community.

A key part of this public disclosure is a series of community meetings being held to inform the public about the proposed research project and its potential to save lives. All community members and hospital staff are invited to join the Allegheny MCP physicians conducting the research study – Thomas Santora, M.D., Associate Professor of Surgery, Associate Director of The Regional Resource Trauma Center, and Vincent Cowell, M.D., Instructor in Anesthesiology and Trauma Anesthesiologist– who will explain the nature of the study, outline the risks and benefits of the study, discuss the concept of exception to informed consent, present patient and community safeguards that have been put in place, and answer questions.

The meetings have been scheduled for:

- **Friday, April 11, at 7 p.m.,** at Devereaux United Methodist Church, 26th and Allegheny Avenue, Philadelphia
- **Wednesday, April 16, at 7 p.m.,** at Falls of Schuylkill Library, located at Warden Drive and Midvale Avenue, Philadelphia
- **Thursday, April 17, at 7 p.m.,** at C.E. Picket Middle School, located at Wayne and Chelten Avenue, Philadelphia

Faculty, staff, employees and students are welcome to attend these meetings and give valuable input. Research concerning severely injured patients could one day save your life or the life of someone you love. ◆

New Monthly EAP Parenting Support Group Formed

The Employee Assistance Program (EAP) has created a new parenting support group that will meet during lunchtime on a monthly basis. The group will provide support for parents and grandparents who are caring for children of all ages.

Topics will include:

- How to stretch your time with your kids
- Ways to be creative with your kids
- At what age should kids get certain responsibilities
- Areas of interest or concern you may have as a parent
- Basic exchanges of ideas for parents

The first meeting will take place Friday, April 25, from noon to 1 p.m. in the President's Conference Room on the fifth floor of the hospital. Bette Begleiter, mother of three, EAP Manager, will facilitate the discussion. For more information, call 842-4690. ◆

More than 30 employees, including Sylvia Beck, M.D. (left), Ophthalmology, received free dexa screenings as part of the new Osteoporosis Program at Allegheny MCP. Kendra Zuckerman, M.D. (right), Director of the Osteoporosis Program, interpreted results

Allegheny Cardiovascular Institute to Hold Annual Night at the Races

Enjoy a lively evening with friends at the Allegheny Cardiovascular Institute tenth annual Night at the Races Friday, May 2, at Garden State Park, Route 70 and Haddonfield Road, Cherry Hill, N.J.

Tickets for the event are $60 per person and include a deluxe buffet dinner, admission to the park, Phoenix valet parking, Phoenix admission and a racing program. Doors open at 6:30 p.m.; post time is 7:30 p.m. Gentlemen are required to wear jackets.

The Allegheny Cardiovascular Institute is a newly constituted organization to advise, counsel and support the cardiovascular endeavors of Allegheny Health, Education and Research Foundation. The organization is committed to advancing cardiovascular research, education and patient care.

For ticket information, please call Mari-

Attachment 24

Working Through the Public Disclosure Process Mandated by Use of 21 CFR 50.24 (Exception to Informed Consent): Guidelines for Success

Thomas A. Santora, M.D.*, Vincent S. Cowell, M.D., Stanley Z. Trooskin, M.D.* Allegheny University of the Health Sciences-MCP, Department of Surgery, Division of Trauma & Surgical Critical Care, Philadelphia, PA

Introduction In November 1996, the FDA formalized guidelines for emergency care research to be done under an "exception to informed consent". These guidelines (21 CFR 50.24) mandate community awareness of the proposed research, but provide no specific methods by which to accomplish this task. This descriptive report outlines how our Level I Trauma Center established a community educational program for a study utilizing a blood substitute.

Methods A counsel of leaders from the highest volume trauma communities (HVTC) was established to review the research project and assist in development of our public disclosure (PD) program. Hospital personnel were educated through faculty meetings, hospital committees, in-house publication feature articles and flyers. The community was informed of our intent, purpose and issues related to this research project by a talk radio show, radio public service announcements, advertisements and feature articles in local and regional newspapers. Additionally, three interactive education meetings were held in the HVTC. A call-in line was established for community feedback.

Results An excess of 70 manpower hours were required for our PD. All communities acknowledged the gravity of the problem faced by the severely injured patient. Initial skepticism was encountered about the motivation of the institution to involve the community in hospital activities, the safety of the experimental product, the minority population shouldering an unfair proportion (Tuskegee fallout) of the research burden and the loss of individual decision-making liberty. Though universal community acceptance of this research study was not achieved, the educational process diminished the majority of the community's suspicions.

Conclusions Though PD of clinical research is difficult and time-consuming, the results can be rewarding. The investigator(s) must identify the community, open lines of communication and be prepared for skepticism. The PD mandate of 21 CFR 50.24 to increase community awareness was met through extensive honest and forthright information exchange.

Thomas A. Santora, M.D., Assoc. Prof. of Surgery, Allegheny University of the Health Sciences-MCP, Dept. of Surgery, Div. of Trauma & Surg. Crit. Care.
3300 Henry Avenue, Philadelphia, PA 19129 (215) 842-6567

Thomas A. Santora, MD

Contact: Eryn Dobeck
Ruth Ann Dailey
(215) 842-4533

NEW ADVANCEMENTS IN TRAUMA CARE FOR YOUR COMMUNITY

PSA :15

EACH YEAR CLOSE TO 140,000 PEOPLE DIE AS A RESULT OF TRAUMATIC INJURY. IN MANY CASES, BLOOD LOSS IS THE CAUSE OF DEATH. RESEARCH WITH A NEW BLOOD SUBSTITUTE IS BEING CONDUCTED AT ALLEGHENY UNIVERSITY HOSPITALS, MCP. THIS RESEARCH COULD SAVE YOUR LIFE. FOR INFORMATION, CALL 1-800-PRO-HEALTH.

-30-

Attachment 26

05 PSA Radio/TV

11-1-94

000-000152

MR #

Subject:

Send on PR Newswire?

Send to Provider Plan List?

Mailing Date:

Public Service Director
KYW-RADIO
Independance Mall East
Philadelphia, PA 19106

Public Service Director
KYW-TV
Independence Mall East
Philadelphia, PA 19106

NJN Radio
The New Jersey Station
CN 777
Trenton, NJ 08625-0777

Public Service Director
RADIO INFORMATION FOR THE BLIND
919 Walnut Street
Philadelphia, PA 19107

The PSD News Center/ERC-TC
THE PA SCHOOL FOR THE DEAF
100 West School House Lane
Philadelphia, PA 19144

Public Service Director
WBCB
200 Magnolia Drive
Box 1490
Levittown, PA 19054

Public Service Director
WBUX
P.O. Box 2187
Doylestown, PA 18901

Public Service Director
WBYO-FM
P.O. Box 177
Boyertown, PA 19512

Public Service Director
WCAU-TV
City Line Ave./Monument Rd.
Philadelphia, PA 19131

Public Service Director
WCHE
119 Market Street
West Chester, PA 19382

Public Service Director
WCHR-FM
Woodside Road
Yardley, PA 19067

Public Service Director
WCOJ
P.O. Box 1408
Coatesville, PA 19320

Public Service Director
WDAS-AM & FM
WDAS Building
Belmont Avenue & Edgeley Rd.
Philadelphia, PA 19131

Public Service Director
WDRE-FM
P.O. Box 1188, Suite A-104
Benjamin Fox Pavilion
Jenkintown, PA 19046

Public Service Director
WEAZ-FM
Philadelphia Executive Offices
10 Presidential Blvd.
Bala Cynwyd, PA 19004

Public Service Director
WEGX-FM
3 Bala Plaza
Suite 580E
Bala Cynwyd, PA 19004

WEXP, LA SALLE UNIVERSITY
C/o Promotions
P.O. Box 698, 20th & Olney Ave
Phila.,, PA 19141

Public Service Director
WFIL
10 Presidential Blvd.
Bala Cynwyd, PA 19004

Public Service Director
WFLN
8200 Ridge Avenue
Philadelphia, PA 19128

Public Service Director
WFMZ-FM
East Rock Road
Allentown, PA 18103

Public Service Director
WGLS-FM
Glassboro State College
Glassboro, NJ 08028

Public Serv. Dir.
WHAT
KBT Communications
2471 N. 54th Street
Philadelphia, PA 19131
(215) 581-5161

Public Service Director
"HWH
.O. Box 9750
Trenton, NJ 08540

Public Service Director
WHYY-FM
Independence Mall West
150 North 6th Street
Philadelphia, PA 19106

Public Service Director
WHYY-TV
Independence Mall West
Philadelphia, PA 19106

Public Service Director
WIOQ-FM
2 Bala Plaza
Suite 201
Bala Cynwyd, PA 19004

Public Service Director
WIP
441 North Fifth Street
Philadelphia, PA 19123

Public Service Director
WJBR-FM
2617 Elbright Road
Wilmington, DE 19810

Public Service Director
WKDN-FM
2906 Mt. Ephraim Avenue
Camden, NJ 08104

Public Service Director
WMGK-FM
1 Bala Plaza
3rd Floor West
Bala Cynwyd, PA 19004

Public Service Director
WMMR-FM
19th & Walnut Streets
Philadelphia, PA 19103

Public Service Director
WNAP
Box 11
Philadelphia, PA 19128

Public Service Director
WNJS-TV
1573 Parkside Avenue
Trenton, NJ 08638

Public Service Director
WNPV
Snyder Road
Box 1440
Lansdale, PA 19446

Public Service Director
WOGL-AM/FM
City Line Ave./Monument Rd.
Philadelphia, PA 19131

Public Service Director
WPAZ
Maugers Mill Road
Box 638
Pottstown, PA 19464

Public Service Director
WPEN
1 Bala Plaza
3rd Floor West
Bala Cynwyd, PA 19004

Public Service Director
WPHL-TV
5001 Wynnefield Avenue
Philadelphia, PA 19131

Public Service Director
WPST-FM
Box 9750
Trenton, NJ 08607

Public Service Director
WPVI-TV
4100 City Line Avenue
Philadelphia, PA 19131

Public Service Director
WRTI-FM
TEMPLE UNIVERSITY
Annenberg Hall
Philadelphia, PA 19122

Public Service Director
WSSJ
6th & Market Streets
Camden, NJ 08101

Public Service Director
WSTW-FM
2727 Shipley Road
Wilmington, DE 19803

Public Service Director
WTEL
1349 Cheltenham Avenue
Philadelphia, PA 19126

Public Service Director
WTMR
2775 Mt. Ephraim Avenue
Camden, NJ 08104

Public Service Director
WTTM
333 West State Street
Trenton, NJ 08618

Public Service Director
WTXF-TV
4th & Market Streets
Philadelphia, PA 19106

Public Service Director
WUSL-FM
440 Domino Lane
Philadelphia, PA 19128

Public Service Director
WVCH
P.O. Box A
Brookhaven, PA 19015

Public Service Director
WWDB-FM
166 E. Levering Mill Rd.
Bala Cynwyd,, PA 19004

Public Service Director
WXPN-FM
3905 Spruce Street
Philadelphia, PA 19104

Public Service Director
WXTU-FM
23 West City Line Avenue
Bala Cynwyd, PA 19004

Public Service Director
WYSP-FM
1 Bala Plaza
Suite 424
Bala Cynwyd, PA 19004

Jerry Abear
News Director
WYXR-FM
One Bala Plaza
Bala Cynwyd, PA 19004

Public Service Director
WYXR-FM
One Bala Plaza
Bala Cynwyd, PA 19004

Public Service Director
WZZD
117 Ridge Pike
Lafayette Hill, PA 19444

000-000157

06. PSA-Cable TV
11-1-94

NR #
Subject:
Mailing Date:

Public Service Director
ADELPHIA CABLE
P.O. Box 198
1 Apollo Rd.
Plymouth Meeting, PA 19462

Public Service Director
AMERICAN CABLEVISION OF PA
3 Moore Road
Wallingford, PA 19086

Public Service Director
CABLE TV OF CHESTER CO.
Rt. 82 & Monacy Road
Coatesville, PA 19320

Public Service Director
CATV SERVICE COMPANY
46 North Union Street
Lambertville, NJ 08530

Public Service Director
COMCAST CABLEVISION
29 York Road
Willow Grove, PA 19090

Public Service Director
GREATER PHILA. CABLEVISION
1351 South Delaware Avenue
Philadelphia, PA 19147

Public Service Director
HARRON CABLE TELEVISION
First & Ruthland Avenues
Malvern, PA 19355

Public Service Director
HOME-VUE CABLE TV
4143 Swamp Road
Doylestown, PA 18901

Public Service Director
JONES INTERCABLE, INC.
Box 775
Turnersville, NJ 08012

Public Service Director
LOWER BUCKS CABLEVISION
2320 Trenton Road
Levittown, PA 19056

Public Service Director
MAPLE SHADE CABLE TV
60 West Main Street
Maple Shade, NJ 08052

Public Service Director
NYT CABLE-TV
1250 Haddonfield-Berlin Road
Box 5025
Cherry Hill, NJ 08034

Public Service Director
OXFORD VALLEY CABLEVISION
1750 Byberry Road
Bensalem, PA 19020

Public Service Director
PENN STATE CABLE
114 Ridge Road
Sellersville, PA 18960

Public Service Director
SERVICE ELECTRIC CABLE
1045 Hamilton Street
Allentown, PA 18101

Public Service Director
STORER CABLE COMMUNICATION
Box 50
Willingboro, NJ 08046

Public Service Director
STORER COMMUNICATIONS OF
GLOUCESTER COUNTY
304 South Broad Street
Woodbury, NJ 08096

Public Service Director
STORER RIVERFRONT CABLE
1809 Taylors Lane
Cinnaminson, NJ 08077

Public Service Director
SUBURBAN CABLE
237 West Germantown Pike
Norristown, PA 19401
610-239-2100

Public Service Director
SUBURBAN CABLE TV
2319 York Rd.
Jamison, PA 18929

Public Service Director
SUBURBAN CABLE TV COMPANY
114 Ridge Road
Sellersville, PA 18960

Public Service Director
SUBURBAN CABLE TV COMPANY
20 South Main Street
Phoenixville, PA 19460

Public Service Director
SUBURBAN CABLE TV COMPANY
601 Oak Lane
Glenolden, PA 19036

Public Service Director
SUBURBAN CABLE TV COMPANY
503 South Cedar Lane
Upper Darby, PA 19082

Public Service Director
SUBURBAN CABLE TV COMPANY
3 Moore Rd.
Wallingford, PA 19086

Public Service Director
SUBURBAN CABLE TV COMPANY
261 West DeKalb Pike
Suite EG2
King of Prussia, PA 19406

Public Service Director
SUBURBAN CABLE TV COMPANY
1200 High Street
Pottstown, PA 19464

Public Service Director
TCI OF NEW JERSEY
520 Monmouth Street
Gloucester, NJ 08030

Public Service Director
ULTRACOM OF LANSDALE, INC.
668 Bethlehem Pike
Montgomeryville, PA 18936

Attachment 27

MEMORIAL JOINS NATIONAL TRAUMA RESEARCH STUDY

June 12, 1997

Memorial Medical Center, Inc., is one of about 30 sites nationwide chosen to study the effectiveness of a new blood substitute that possibly could save the lives of trauma patients with severe blood loss. The oxygen-carrying hemoglobin solution is part of a new group of blood substitutes having many potential applications and affecting millions of people. Every year, nearly 1.2 million people sustain severe traumatic injuries. More than 150,000 of these people die, making trauma-related injuries the number one cause of death among Americans ages 1 through 45.

Memorial's research study will test the effectiveness and safety of the blood substitute, **Diaspirin Cross Linked Hemoglobin** (DCLHb), in treating patients with serious traumatic hemorrhagic shock (severe blood loss due to serious injury). Nationwide, a total of 850 patients will be enrolled in this clinical trial. The study is expected to last approximately a year and is sponsored by Baxter Healthcare Corporation. Memorial has been chosen to participate due to the presence of research staff, trauma team, nurses, and lab technicians to support this type of research.

Memorial Medical Center would like to make participation in this study available to its patients who suffer from severe traumatic hemorrhagic shock, even when it is not possible to get informed consent from a family member or legal guardian prior to giving the blood substitute. Accordingly, Memorial Medical Center is taking this opportunity to communicate with the community and inform potential patients, guardians, and other appropriate parties of the potential use of this new product.

Between 10 and 20 patients will be enrolled in the study at Memorial. Half will receive the blood substitute and half will receive a saline solution. In addition, current standard treatment, including blood transfusion when appropriate, will be administered to all study participants.

The blood substitute is man-made and derived from human red blood cells which would otherwise be wasted. It has potential applications in situations where large amounts of blood loss can result in a lack of oxygen to vital tissues. Patients can go into shock, which can lead to multiple organ failure several days or weeks after the initial injury. The blood substitute has been shown to carry oxygen to cells and tissues and seems to increase blood flow to vital organs.

Use of the blood substitute as a supplement to blood transfusions also saves critical time in stabilizing a badly hurt patient because it does not have to be typed or cross-matched. The solution has been heated and filtered to reduce the risk of blood-borne infections. The blood substitute has been studied extensively over a four year period in clinical trials involving more than 700 patients. Of the approximately 350 who received the drug, a few temporary side-effects were noted. These included changes in some lab test results, a temporary yellowing of the skin (unrelated to liver damage), temporary reddening of the urine due to the red color of the product, nausea, and back, abdominal and muscle pain. Blood pressure may be elevated following administration.

Because trauma patients are often so severely injured, they may not be able to give consent to participate in the drug trial, and family frequently cannot be located or reached quickly. For this reason, the U.S. Food and Drug Administration and the Office of Protection of Patient Rights allows waiving consent in studies of emergency therapies when the potential benefits outweigh the risks. It is critical in trauma situations that the blood substitute be given within the first hour that the patient is being treated. Once the families are found, they will be informed of the study and can decide on continued participation.

Media inquires should be made to Derek Smith, MMC Corporate Communications, at (912) 350-6874.

Attachment 28

AIKEN COMMUNITY HOSPITAL
ER NURSE MANAGER
P.O. 1117
AIKEN, SC 29802

ALLENDALE CO.HOSPITAL
ER NURSE MANAGER
P.O. BOX 216
FAIRFAX, SC 29827

APPLING GENERAL HOSPITAL
ER NURSE MANAGER
301 E. TOLLISON ST.
BAXLEY, GA 31513

BACON HOSPITAL
ER NURSE MANAGER
P.O. BOX 745
ALMA, GA 31510

BAMBERG CO MEM HOSP.
ER NURSE MANAGER
NORTH & MCGEE STS.
BAMBERG, SC 29003

BARNWELL CO. HODPITAL
ER NURSE MANAGER
P.O. BOX 588
BARNWELL, SC 29812

BEAUFORT MEMORIAL HOSP.
ER NURSE MANAGER
121 RIBAUT RD.
BEAUFORT, SC 29902

BEAUFORT NAVAL HOSPITAL
ER NURSE MANAGER
RIBAUT RD.
BEAUFORT, SC 29902

BERRIEN CO. HOSPITAL
ER NURSE MANAGER
P.O. BOX 665
NASHVILLE, GA 31639

BULLOCH MEM. HOSP.
ER NURSE MANAGER
P.O. BOX 1048
STATESBORO, GA 30458

BURKE COUNTY HOSP.
ER NURSE MANAGER
351 LIBERTY ST.
WAYNESBORO, GA 30830

CANDLER COUNTY HOSP.
ER NURSE MANAGER
P.O. BOX 597
METTER, GA 30439

CANDLER GEN. HOSPITAL
ER NURSE MANAGER
5353 REYNOLDS ST.
SAVANNAH, GA 31404

CHARLTON MEM. HOSPITAL
ER NURSE MANAGER
P.O. BOX 166
FOLKSTON, GA 31537

CLINCH MEMORIAL HOSP.
ER NURSE MANAGER
P.O BOX 516
HOMERVILLE, GA 31634

COFFEE REG. HOSPITAL
ER NURSE MANAGER
P.O. BOX 1248
DOUGLAS, GA 31533

COLLETON REGIONAL HOSP.
ER NURSE MANAGER
501 ROBERTSON BLVD.
WALTERBORO, SC 29488

DODGE COUNTY HOSPITAL
ER NURSE MANAGER
715 GRIFFIN ST.
EASTMAN, GA 31023

EFFINGHAM COUNTY HOSP.
ER NURSE MANAGER
P.O. BOX 386
SPRINGFIELD, GA 31329

EMANUEL COUNTY HOSP.
ER NURSE MANAGER
P.O. BOX 7
SWAINSBORO, GA 30401

EVANS MEMORIAL HOSP.
ER NURSE MANAGER
P.O. BOX 518
CLAXTON, GA 30417

FAIRVIEW PARK HOSPITAL
ER NURSE MANAGER
200 INDUSTRIAL BLVD.
DUBLIN, GA 31201

HAMPTON GENERAL HOSP.
ER NURSE MANAGER
P.O.B. 336
VARNVILLE, SC 29944

HILTON HEAD HOSPITAL
ER NURSE MANAGER
P.O.B. 1117
HILTON HEAD, SC 29925

JEFF DAVIS HOSPITAL
ER NURSE MANAGER
1215 S. TALLAHASSEE ST.
HAZLEHURST, GA 31539

JEFFERSON HOSPITAL
ER NURSE MANAGER
PEACHTREE ST.
LOUISVILLE, GA 30434

JENKINS COUNTY HOSPITAL
ER NURSE MANAGER
515 E. WINTHROPE AVE.
MILLEN, GA 30442

LIBERTY REG. MED. CNTR.
ER NURSE MANAGER
P.O.B. 232
HINESVILLE, GA 31313

LOW COUNTRY GENERAL
ER NURSE MANAGER
POB 400
RIDGELAND, SC 29936

MEADOWS REGIONAL MED.
ER NURSE MANAGER
POB 1048
VIDALA, GA 30474

MED. CNTR. OF CENTRAL GA
ER NURSE MANAGER
HEMLOCK ST.
MACON, GA 31208

MEMORIAL MEDICAL CENTER
ER NURSE MANAGER
4700 WATERS AVE.
SAVANNAH, GA 31406

ORANGEBORG REG.MED. CTR.
ER NURSE MANAGER
3000 ST. MATTHEWS RD.
ORANGEBORG, SC 29115

PHOEBE PUTNEY MEM HOSP
ER NURSE MANAGER
417 3RD. AVE
ALBANY, GA 31701

PIERCE COUNTY HOSPITAL
ER NURSE MANAGER
POB 32
BLACKSHEAR, GA 31516

SCREVEN COUNTY HOSPITAL
ER NURSE MANAGER
215 MIMS RD.
SYLVANIA, GA 30467

ST. LUKE'S
ER NURSE MANAGER
4201 BELFORT RD.
JACKSONVILLE, FL 32216

ST. JOSEPH'S HOSPITAL
ER NURSE MANAGER
11705 MERCY BLVD.
SAVANNAH, GA 31419

TATTNALL MEMORIAL HOSP.
ER NURSE MANAGER
RT. 1, BOX 204
REIDSVILLE, GA 30453

TELFAIR COUNTY HOSPITAL
ER NURSE MANAGER
RT. 1, BOX 5
MCRAE, GA 31055

TRIDENT REG. MED. CNTR.
ER NURSE MANAGER
9330 MEDICAL PLAZA DRIVE
CHARLESTON, SC 29418

UNIVERSITY HOSPITAL
ER NURSE MANAGER
1350 WALTON WAY
AUGUSTA, GA 30910

WASHINGTON COUNTY HOSP.
ER NURSE MANAGER
POB 636
SANDERSVILLE, GA 31082

WAYNE MEMORIAL HOSPITAL
ER NURSE MANAGER
POB 408
JESUP, GA 31545

WHEELER COUNTY HOSPITAL
ER NURSE MANAGER
3RD STREET
GLENNWOOD, GA 30428

WINN ARMY COMM. HOSP.
ER NURSE MANAGER
FT. STEWART, GA 31314

Attachment 29

MEMORIAL MEDICAL CENTER STUDIES NEW TREATMENT for PATIENTS WITH SEVERE BLOOD LOSS

Memorial Medical Center, Inc. has been asked to evaluate a new treatment for seriously injured patients admitted to its Emergency Room with severe loss of blood. The new treatment, a patented product developed by Baxter Healthcare, Inc., has potential as a blood sustitute during the emergency treatment and recovery period. Patients enrolled in the study will also receive standard treatment including blood transfusions.

The U.S. Food and Drug Administration requires new drugs and therapies to be proven effective with volunteer human patients before approval for marketing. The FDA has ruled that a patient whose life is in danger, is unable to consent, and for whom there is no one available to give consent may be given an experimental treatment when the potential benefits outweigh the risks. Patients or their families will be notified at the earliest opportunity of the patients' inclusion in the research study.

Memorial Medical Center would like to make participation in this study available to its patients who suffer from severe traumatic hemorrhagic shock, even when it is not possible to get informed consent from a family member or legal guardian prior to giving the blood substitute. Accordingly, Memorial Medical Center is taking this opportunity to communicate with the community and inform potential patients, guardians, and other appropriate parties of the potential use of this new product.

Public input is welcome. To communicate with us on this subject, please write to us at the following address:

Memorial Research Center
Memorial Medical Center
P.O. Box 23089
Savannah, Georgia 31403-3089

THE GEORGIA GUARDIAN

That much can endure and earn its place in history

August 1-7, 1997 25 CENTS

Vol. 6 No. 32

Photo by Russ Bryant

Several area physicians are at the forefront of modern medical procedures, including synthetic blood and cancer treatments.

Cutting-edge medical technology in Savannah

By Francis Zera

While some may think Savannah's small-town atmosphere may limit the availability of the newest medical treatments, several area physicians are currently offering state-of-the-art techniques to the region.

Dr. Frank Davis, Dr. John Duttenhaver and Dr. Ray Rudolph, all of whom work out of Memorial Medical Center, each offer their patients a unique form of treatment that either dramatically increases their patients' survival rates or reduces the discomfort and cost of treatment.

Memorial Medical Center's trauma center is one of only 30 hospitals nationwide that is participating in a study to test a new blood substitute, Diaspirin Cross-Linked Hemoglobin, in treating patients with serious traumatic hemorrhagic shock, which is caused by dramatic blood loss due to serious injury. Davis, as chief of trauma services, oversees the program.

The blood substitute, explained Davis, is synthesized from donated blood that has reached the end of its shelf life. "The hemoglobin molecules are taken out of the blood, linked together, diseases are eliminated, then is prepared to be frozen for up to two years." Donated accurate method for detecting potentially cancerous lumps using an in-office ultrasound device.

"Until a couple of years ago," said Rudolph, "all ultrasounds of breast tissues were done by a radiologist."

"The difference is that if you come to the office and have an abnormality but can't feel it, within 20 minutes I can tell if it's cancer or not, as opposed to waiting until the next day for traditional methods," he said. A biopsy of suspected cancerous tissues can be done with a needle, guided by an ultrasound monitor. "That way, we can talk about it right away, as opposed to putting the patient to sleep, doing a surgical biopsy, waiting for them to wake up and then trying to discuss the implications," he said. "This is much more expedient."

"There is no known cause and no known cure for breast cancer," Rudolph said. "The whole essence of breast cancer is that women who have long survival rates are the ones who have had their cancer detected early."

The best way to increase detection of breast cancer, according to Rudolph, is self-examination, regular clinical exams and annual mammograms starting at age 40.

In men, prostate cancer is as prevalent as breast cancer is in women, Duttenhaver said. It's the

The Bus Stops Here 1997-98 public school bus schedule inside this issue.

Section C.

Getting Their Feet Wet Savannah area Olympian offers inspiration to budding swimmers. Page 5A.

Complementary! SCAD painting students explore two different sides of large-format drawings. Page 1B.

Red Cross for diseases including HIV, AIDS and hepatitis. Blood used for the substitute is put through a heat process to eliminate any undetected diseases.

Among the benefits of the synthesized blood, said Davis, include its being free of blood-borne diseases, a long storage life, and, most importantly, the ability to use it with patients of any blood type. "Because you get rid of the red blood cells, there are no compatibility problems," he said.

"This is only for the sickest of the sick," explained Davis. "The people who participate in this study will be multi-system trauma victims who have lost at least 40 percent of their blood volume — only 10 or 20 patients will qualify for the study" over its one-year duration.

Based on the results of the study, the substitute could be generally available within three years. "This might not eliminate the need to give blood, but will help greatly with victims of acute trauma," he said.

Breast cancer will strike one in every nine women in the United States, and 32 percent of women who die from cancers each year die from breast cancer. In response to those statistics, vast amounts of time and money are being spent researching ways to beat breast cancer. Rudolph offers a non-invasive, men, accounting for one-third of cancers diagnosed each year.

Duttenhaver said that, in the past, the effectiveness of treatment was limited by the amount of radiation that was able to be transmitted to the cancerous gland. A new treatment called radioactive seed implant therapy holds lots of promise for increasing cure rates for this type of cancer.

"The key to curing cancer is getting the highest dose of radiation to the cancer," Duttenhaver said.

He said that prior to the introduction of implant therapy, the amount of radiation that could be used to treat prostate cancer was limited by the propensity for the organs and tissues surrounding the prostate gland to absorb excess radiation, potentially causing complications such as radiation burns.

The new technique involves introducing radioactive pellets, or seeds, into the prostate gland, precisely placing them near the cancerous tissues with a needle guided by an ultrasound monitor. The seeds are designed to emit radiation for two to six months, becoming inert within a year. "By placing the seeds precisely within the gland, we can double the dose to 16,000 rads (radiation absorbed dose, a standard radiation measure), which pushes the cure rate up to nearly 90 percent," he said.

Attachment 31

THE GEORGIA GUARDIAN
That truth can endure and earn its place in history

August 8-14, 1997/page 7A

goals for student and teacher alike. further, submitting such a paper

Letter to the Editor

MMC research coordinator expands on study policy

Thank you for the very positive article in the Aug. 1-7, 1997 Georgia Guardian, "Cutting-edge Medical Technology in Savannah."

In order to implement the protocol which Francis Zera described in his interview with Dr. Frank Davis, the FDA has approved this particular study (the use of a synthetic blood substitute in victims of severe trauma) to have "deferred consent." This means the drug can be administered immediately without the usually lengthy and intense process of obtaining consent from the patient or family. The administration of the diaspirin drug must be finished within 60 minutes of the patient arriving in the emergency room, and there are numerous lab and other diagnostic procedures to be completed before the administration of the drug product. Also, on many occasions, unresponsive or otherwise not responsible patients arrive at the ER alone and without clear information on how to contact their families immediately.

Therefore, the FDA has granted this special privilege (of deferring the consent process) to Memorial Medical Center and the other hospitals participating in the study, with the proviso that informed consent will be obtained as soon as possible. With these "total body crunch" patients who have suffered severe, multiple trauma with hemorrhage, this almost always means that the responsible family member will be the person to sign the form, after being comprehensively advised of benefits and risks by one of the physicians in the study.

This responsible person has the unimpeded choice at that time to state that the study may not continue and he or she is so advised that this decision will be honored immediately without prejudicing any other alternative treatments or affecting the patient's care in any adverse manner. Of course, the responsible person also has the choice to allow the patient to continue in the study. The procedures after the initial administration of the drug are no more than "following" the patient to see how his or her condition fares for the following 28 days after admission. Some lab work is involved, but charges for these tests, as well as for the drug itself, are paid for by the sponsoring drug company, Baxter Laboratories. Administration of the drug is not, under any circumstances, repeated after the initial dosage.

Earl Stanford, RN BSN CCRC
Certified Clinical Research Coordinator
Research Center
Memorial Medical Center

Attachment 32

Newscast, July 15, 1997
Channel 3, WSAV, NBC affiliate
Savannah, GA

Introduction: News anchors introduced product as a "...new blood substitute which can save lives. Some experts believe it may be better than the real thing."

Segway to Family Health Reporter, Kristin Hill at " Memorial Medical Center where the product is being tested."

Kristin Hill: "You're rushed into the emergency room with a serious injury. You've lost a lot of blood and are going into shock. You need blood fast but typing and checking for antibodies takes time. Using a new blood substitute made from outdated blood could save time and your life."

Dr. Gage Ochsner, Chief of Trauma Services, Memorial Medical Center explains: "The solution is given through the vein and early on. Patients who get this are given it within 30 minutes of arrival."

Kristin Hill: "When Life Star (helicopter) or an ambulance brings in a trauma patient, using the blood substitute can save critical amounts of time because blood typing is not necessary and the blood product can be stored in the emergency room. Memorial Medical Center is taking part in National test trials."

Dr. Ochsner: "We will be giving solution to patients who have a 40% chance of dying or greater because of blood loss."

Kristin Hill: "Memorial will enroll 10-20 patients in the study. Prior consent is not required by FDA for a patient to receive the blood solution."

Dr. Ochsner: "FDA has authorized use because of the potential benefit of using this outweighs the risk associated with it."

Kristin Hill explains: As the blood substitute carries oxygen to cells and tissues it increases blood flow to vital organs just like real blood, but keeps longer, and when given with real blood it may mean better survival rates and fewer complications for trauma patients.

Closing: Program ends with the following message. "For more information on the study call Memorial Medical Center Trauma Research Study, Phone number 912 350-8707."

Attachment 33

Clinical Trial of Diaspirin Cross-Linked Hemoglobin
Emergency Treatment of Patients in Shock

Memorial Medical Center is among 35 major trauma centers that are evaluating a new treatment for critically injured patients with severe blood loss. The treatment involves administering an experimental blood product to such patients, who face a major risk of dying despite the best medical care. Baxter Healthcare, Inc., has developed the product, Diaspirin Cross-linked Hemoglobin (DCLHb™), which is being tested during the emergency treatment of trauma patients in shock. The trial, which is authorized by the U.S. Food and Drug Administration, requires public notice because it will occur under emergency conditions that may require an exception from informed consent. The following is to help to prepare you to answer potential questions about the trial.

Q. Why is this trial being performed?

A. Seriously injured patients frequently arrive at the hospital in shock with significant blood loss. Despite the best care medicine has to offer, as many as 40 percent of the most critically injured patients will die from their injuries. Studies suggest that DCLHb™ may improve the chance of survival following severe blood loss. The product has the greatest chance of improving survival and reducing complications when it is given immediately after the beginning of catastrophic shock and bleeding.

Q. What is DCLHb™?

A. DCLHb™ is a purified hemoglobin (the part of blood that carries oxygen) preparation made from human blood that has become outdated on blood bank shelves and is no longer usable for transfusions. It is filtered and heated to reduce the risk of blood-borne infections including AIDS. DCLHb™ may restore blood pressure, increase blood flow to vital organs and carry oxygen to cells and tissues. Because blood typing is not required and the product can be stored in the Emergency Department, DCLHb™ can be given immediately after a patient's arrival, saving critical moments in stabilizing a trauma-patient.

Q. Does DCLHb™ replace the need for blood transfusion?

A. DCLHb™ is administered in addition to transfusions that may be needed to treat the injured patient. (Since the product is made from human blood, it would not be suitable in treating patients whose religious beliefs forbid blood transfusions.) Patients will still get all standard therapies in this study, including blood, fluids and surgery. Although DCLHb™ may reduce the number of blood transfusions required to treat the injured, volunteer blood donations are still vital.

Q. What is an exception from informed consent and why is it necessary?

A. Because trauma patients are often so severely injured, they may not be able to give their consent to participate in the drug trial. Still, they are in critical need of immediate treatment. The U.S. Food and Drug Administration has granted an exception from informed consent in such cases. They have carefully evaluated DCLHb™ and determined that the potential benefits greatly outweigh the risks of participating in the trial. As a result, patients may be enrolled in this study and receive DCLHb™ when informed consent is not possible.

We will make every attempt to obtain consent from patients, their legal representatives, or family before DCLHb™ is given, and all patients and their family members will be completely informed of their participation as soon as possible. At all times, the patient or their representatives may decline further participation in the study. There are no known risks to patients who decide not to continue in the study.

Q. What are the risks and side effects of DCLHb™ ?

A. DCLHb™ has been extensively studied in randomized trials involving more than 700 patients over a four-year period to evaluate its effects. Of the approximately 350 who received the drug, a few temporary side effects were noted. These included changes in some lab test results, a temporary and harmless yellowing of the skin (unrelated to liver damage), temporary reddening of the urine due to the red color of DCLHb™, nausea, and back, abdominal and muscle pain. Blood pressure may be elevated following administration; however, this may be beneficial to patients in shock, whose blood pressure is dangerously low. Independent experts will monitor patient safety throughout the trial.

Q. Who will be eligible to participate?

A. Approximately 30 patients with low blood pressure and in shock from blood loss following traumatic injury will be enrolled at Memorial over the next 18 months. Approximately half of these patients will receive the blood product along with other treatment. This product will be given only to patients who have such major blood loss that standard therapy may not be enough to save their lives. A total of 850 patients will be enrolled nationwide at 35 trauma centers. No additional charges will be incurred by patients as a result of participation.

Attachment 34

For June 16 Notations to physicians:

Dr. Raymond P. Bynoe, Trauma Services, will serve as principal investigator in a study on Diaspirin Cross-Linked Hemoglobin that will begin by August. DCLHb, a man-made hemoglobin solution, will be used in patients suffering traumatic shock from blood loss. Dr. N. John Stewart of Emergency Services will join Bynoe as co-investigator in the study.

RMH is one of 40 hospitals nationwide, and the only one in South Carolina participating in the study. A maximum of 20 patients will be eligible to participate in the study during the next 12 months. For more information, call 434-6418.

FOCUS

Richland Memorial Hospital VOLUME 24 NUMBER 7 JULY 8, 1997

New treatment to be tested at RMH

RMH is one of 40 hospitals nationwide and the first in South Carolina that will begin using a potentially life-saving treatment in August for patients h severe traumatic injury. The ıtment being researched is made from nan red blood cells and is called ıspirin Cross-Linked Hemoglobin ⊃LHb).

"The purpose of the study is to find how well the new hemoglobin ıtion works in treating or preventing harmful effects of blood loss due to er ry, including shock, severe e death," says Dr. Raymond noe, medical director of Trauma vices and principal investigator of the dy. "We hope the use of this product as pplement to our life-saving cedures will improve patient comes.

"Despite our best efforts, about percent of trauma patients with remely low blood pressure die, most of m from bleeding problems. Large ounts of blood loss can result in lack of gen to vital tissues, which can lead to ltiple organ failure. DCLHb may rease blood flow and oxygen to the organs, helping stabilize a ient quicker. Patients in this study still will receive all standard rapies, including blood products, fluids, medications and surgery."

DCLHb is a purified hemoglobin solution, the part of blood that ries oxygen throughout the body. The solution is made from red od cells donated by healthy volunteers who have been tested and nd negative for the viruses that cause hepatitis and AIDS. In lition, DCLHb solution goes through a specialized filtration and pasteurization process to significantly reduce the risk of viral transmission. Because the product is made from human blood cells, it will not be suitable for treating patients whose religious beliefs forbid blood transfusions.

George Fulton

RMH will begin using a potentially life-saving treatment next month for patients with severe traumatic injuries.

"While we're excited about the possibility of this research increasing the survivability of trauma patients, we also are excited about it possibly extending the community's blood supply," says Dr. John Stewart, director of Emergency Services and co-investigator in the research project. "This could help extend our resources nationwide."

The study, which is authorized by the U.S. Food and Drug Administration (FDA), will be randomized. This means half the participants will receive the solution and half will receive saline solution after receiving all standard therapies. Neither the patient nor the doctor will know which solution the patient has been given.

The study will be monitored by an independent data monitoring committee. Trauma patients must meet strict criteria before being given the new treatment. Part of the inclusion criteria includes being 18 years of age or older, evidence of hemorrhage, and low blood pressure. Of the 1,500 patients Trauma Services treats each year, approximately 20 patients will be eligible to receive the new product in the next 12 months through the study.

Employees are invited to attend a news conference about DCLHb at 10:30 a.m., July 8, in Dining Room B.

For more information, call Trauma Services at 6418. ■

EMIER PURCHASING PROGRAM STRENGTHENS UALITY, IMPROVES COST EFFECTIVENESS

Strengthening quality and improving cost effectiveness are mmitments RMH states in its vision statement. One such way contract prices."

According to Garvin, there are some exceptions, such as when

News Release Focus

New Treatment to be Tested at RMH

RMH is one of 40 hospitals nationwide and the first in South Carolina that will begin using a potentially life-saving treatment in August for patients with severe traumatic injury. The treatment being researched is made from human red blood cells and is called Diaspirin Cross-Linked Hemoglobin (DCLHb).

"The purpose of the study is to find out how well the new hemoglobin solution works in treating or preventing the harmful effects of blood loss due to severe injury, including shock, severe illness or death," says **Dr. Raymond Bynoe**, medical director of Trauma Services and principal investigator of the study. "We hope the use of this product as a supplement to our life-saving procedures will improve patient outcomes.

"Despite our best efforts, about 40 percent of trauma patients with extremely low blood pressue die, most of them from bleeding problems. Large amounts of blood loss can result in lack of oxygen to vital tissues, which can lead to multiple organ failure. DCL Hemoglobin may increase blood flow and oxygen to the organs, helping stabilize a patient quicker. Patients in this study still will receive all standard therapies, including blood products, fluids, medications and surgery."

DCL Hemoglobin is a purified hemoglobin solution, the

part of blood that carries oxygen throughout the body. The solution is made from red blood cells donated by healthy volunteers that have been tested and found negative for the viruses that cause hepatitis and AIDS. In addition, DCL Hemoglobin solution goes through a specialized filtration and pasteurization process to significantly reduce the risk of hepatitis and AIDS. Because the product is made from human blood cells, it will not be suitable in treating patients whose religious beliefs forbid blood transfusions.

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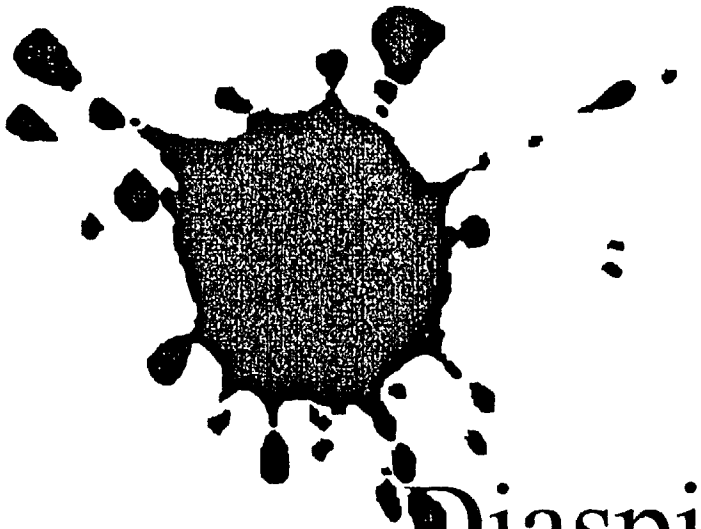
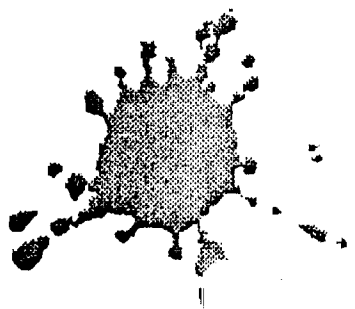
For more information, call Trauma Services at 6418.

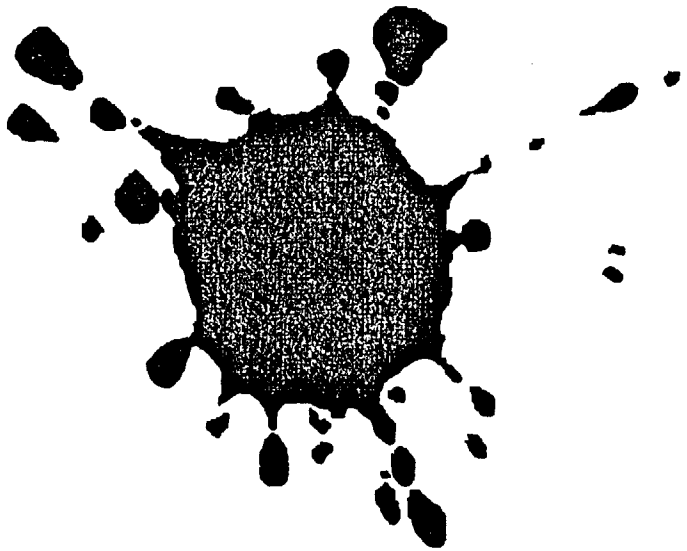
Attachment 36



Diaspirin Cross-Linked Hemoglobin (DCLHb)

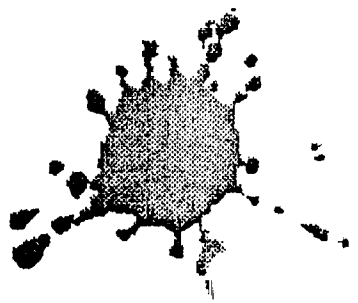
Utilization in the treatment of severe traumatic hemorrhagic shock





Objective

Whether the infusion of DCLHb will reduce the mortality following traumatic hemorrhagic shock



Informed Consent

- FDA approved exception to consent
  - notification of next of kin, legal guardian
- Critically short therapeutic window
- Direct benefit to patients
- IRB
- Notification of Medical community
- Community Education/Information

Randomized Prospective Study

Group One	Group Two
Blood Products plus Placebo	Blood Products plus DCL-Hg

000-000178

Trauma Services - RMH

DCLHb

- Prepared from volunteer donor red cells
- Final 10 % solution
  - contains 10 g of hemoglobin per 100 ml.
  - iso-osmotic with whole blood
  - hyperoncotic
  - adjusted to a pH of 7.4 at 37 degrees C

The 500-1000 ml. study dose provides 50 -100 g of hemoglobin

Inclusion Criteria

- 18 years of age or older
- Evidence of hemorrhage
- Tissue hypoxia & cellular hypoperfusion
  - SBP 90 or less and HR 120 or above OR
  - SBP 90 or less and HR 60 or less with a preterminal rhythm(junctional or idioventricular) OR
  - Base deficit of 15 mmol/L or worse

Exclusion Criteria

- Age less than 18
- Known pregnancy
- Pulseless traumatic arrest during hospitalization
- Imminent death precludes resuscitation efforts
- Isolated head injury, penetrating or blunt
- Known objection to use of blood/blood products
- Known injury time >4 hrs. prior to infusion
- Combined multisystem and head trauma with clinical findings consistent with significant mass effect(e.g.,severe coma, lateralizing signs, posturing or pupil dilation secondary to uncal herniation)
- Hospitalization > 60 min prior to infusion

000-000182

End Points

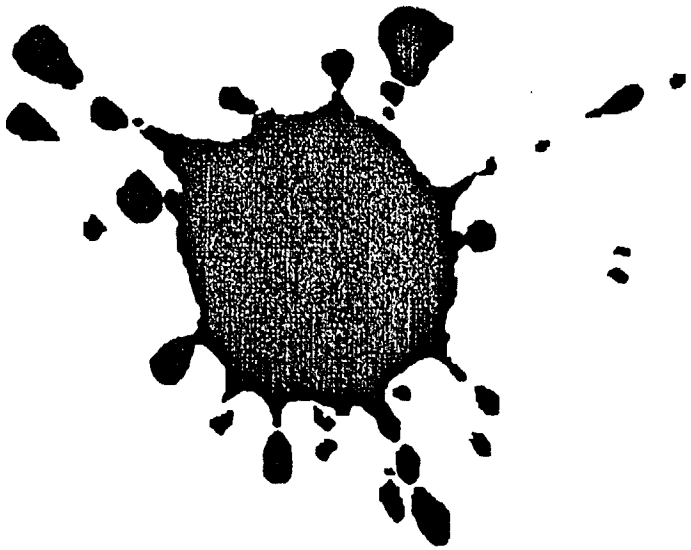
- Primary - Statistically significant reduction in 28 day mortality
- Secondary- 48 hour mortality reduction and Lactate level

DCL Hb Effects

- Increase in mean arterial pressure
  - Dose related response
- Increase organ perfusion
  - Restoration of acid/base balance
- Decreased bacterial translocation
- ? Decrease use of banked blood products

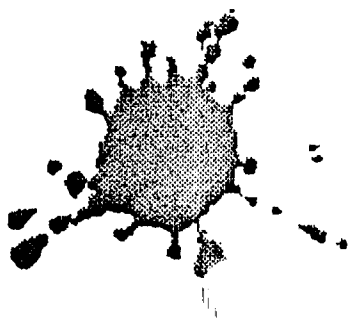
DCL Hb PREPARATION

- Human volunteer blood
- Tested and found negative for HBsAg, HIV-I/II & HCV
- Red cells lysed to release hemoglobin
- Ultrafiltration & reacted with diaspirin x-linked agent
- Stabilized tetrameric hemoglobin
- Pasteurization to effect viral deactivation
- Solution conc. into physiologic vehicle
- Similar to process used to prepare albumin



DCL Hb

HEMOGLOBIN
CONCENTRATION OF PRBC's
20 GM/DL

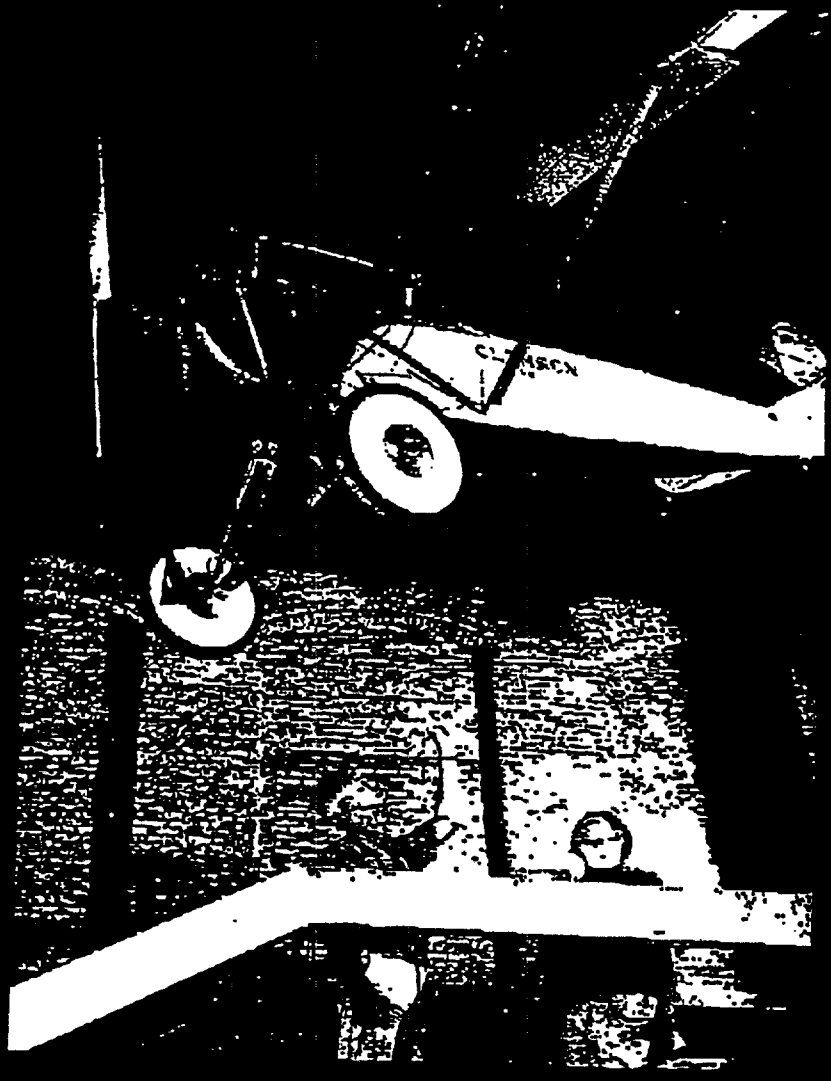


Attachment 37

000-000187

The Recorder

Columbia Medical Society of
Richland County, S.C., Inc.
COLUMBIA, S.C.



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CONTENTS

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Classified Ads: Minimum member rate is $10, non-members $15. Call the Columbia Medical Society office (803-765-1498) for rate information.

The Efficacy Trial of Diaspirin Cross-Linked Hemoglobin (DCLHb) in the Treatment of Severe Traumatic Hemorrhagic Shock

by Raymond P. Bynoe, M.D.

Trauma is the leading cause of death in Americans between the ages of 1 and 44 years, and is surpassed only by cancer and atherosclerosis as a cause of death in all age groups. Approximately 60 million injuries occur each year, and at least half of these people require medical care; of these 30 million injuries, 3.6 million require hospitalization. Trauma is responsible for 145,000 deaths in the USA each year, frequently from shock that is refractory to resuscitation efforts.

The Trauma Service of Richland Memorial Hospital is excited to be able to inform the medical community about the Service's participation in a multi-centered efficacy study about Diaspirin Cross Linked Hemoglobin (DCLHb). DCLHb is a purified human hemoglobin solution that can be utilized in the treatment of severe traumatic hemorrhagic shock. This solution, unlike traditional blood products, does not require cross-matching, and is thus immediately available for infusion in the trauma resuscitation. Blood that has been screened for HIV and Hepatitis viruses is heated and filtered during the pasteurization process to make DCLHb.

DCLHb, in the preliminary studies, has been shown to effectively transport oxygen in vivo as demonstrated by a P50 equal to that of pure human red blood cells. DCLHb has also been shown to optimize vital organ blood flow, prevent tissue hypoxia and lactic acidosis, and ultimately improve survival. DCLHb has also been shown to be effective in small volumes, and thus may improve perfusion in the trauma patient without the untoward effects of large volume crystalloid infusions.

Patients can be enrolled in this efficacy trial if they demonstrate severe shock with signs of hypoperfusion. Patients such as these have a projected mortality rate of 40%. The primary purpose of this study will be to determine whether this infusion can reduce 28 day morbidity and mortality following traumatic hemorrhagic shock.

Approximately twenty patients will be enrolled in the study at RMH over a 12 month period, with at least 800 enrolled in 40 centers nationwide. For additional information on this very promising new solution, please contact Dr. Raymond Bynoe, Dr. Richard Bell or Jay Hamm, RMH Trauma Coordinator, at 434-6418.

VOLUNTEERS NEEDED FOR CMS PROGRAMS

Please call the Society office if you are willing to take part in any of these Society programs:

Mini-Internship Program (see P.14)

Mentoring Program for USC Medical and Pre-Med Students

Anti-Violence Program for at risk school children

Judge entries for CMS awards at the SC Region II Science Fair

For more information call CMS at 765-1498

Attachment 38

June 30, 1997

Community Leader

Dear ,

It is important to recognize that trauma, no matter the cause, has a very high mortality rate and is the leading cause of death for people aged 1-44 years. Trauma is surpassed by only cancer and atherosclerosis as a leading cause of death among all Americans. Approximately 60 million injuries occur each year. At least half of these people require medical care and of the 30 million injured people, 3.6 million have to be hospitalized. Richland Memorial Hospital evaluates over 14,000 patients involved in trauma in the Midlands of South Carolina each year with approximately 1500 admissions.

Trauma is responsible for 145,000 deaths in the United States each year. A major portion of these deaths occur within the first hour following the traumatic event. Many of these deaths are associated with the inability to restore the blood pressure (shock). Despite recent medical and surgical advancements, treatment of life-threatening shock from blood loss secondary to trauma is not always successful.

Trauma Services of Richland Memorial Hospital is excited to announce its participation in a Federal Drug Administration (FDA) approved efficacy trial of Diaspirin Cross-Linked Hemoglobin (DCLHb™) in the treatment of severe traumatic hemorrhagic shock. DCLHb™, a Baxter Healthcare product, is a purified hemoglobin solution made from human blood.The potential advantages of DCLHb™ are: 1) it does not have to be matched to the patient's blood type, 2) it is immediately available for infusion in trauma patients, and 3) it transports and unloads oxygen to the body's cells. The processing of this product effectively reduces the risk of AIDS and other infectious diseases. Testing for carcinogencity for DCLHb™ was not necessary because it is a biological formulation of natural blood protein. Blood, or its products, have never been implicated in causing cancer.

Patients that will be included in the study are trauma patients that have an extremely low blood pressure, (Class III or IV Hemorrhagic Shock) secondary to car or motorcycle crashes, gunshot wounds, stabbings, assaults, or falls. Exclusion criteria include age less than 18 years, pregnancy, or closed head injury. The study will help determine the effectiveness of DCLHb™ in this trauma patient population. All trauma patients enrolled in the study will receive, along with the study solution, all current standard or usual treatments for shock. This may include intravenous solutions, blood and/or blood products, medications, or surgery.

Due to the severity of their injuries, most patients will be unable to give informed consent to participate in this valuable project. However, every effort will be made to obtain informed consent as soon as possible from either the patient or next of kin. The next of kin or legal guardian may withdraw the patient from the study at any time. This procedure follows the FDA's " Exception from Informed Consent Requirements for Emergency Research", #21 CFR 50.24.

Our participation along with 39 other hospitals will give the FDA the appropriate scientific data to evaluate the effectiveness of this new solution, DCLHb™. The study will be monitored by an independent safety group which is not affliliated with Baxter Healthcare or Richland Memorial Hospital. Approximately twenty (20)

trauma patients will be enrolled in this efficacy study at Richland Memorial Hospital over a 12 month period, with at least 850 patients enrolled at the 40 centers nationwide.

In light of an ongoing nationwide blood shortage, Trauma Services of Richland Memorial Hospital sincerely feel that DCLHb™ will not only benefit patients enrolled in the study but will offer a significantly improved chance of survival for many more trauma patients in the future. For additional information on this very promising new solution, please contact Dr. Raymond Bynoe, Dr. John Stewart, or Jay Hamm, R.N. at 803-434-6418. In addition, you are invited to attend a press conference on Tuesday July 8, 1997, in Dining Room B of Richland Memorial Hospital, at 10:30 am.

Sincerely,

Raymond Bynoe, MD, FACS
Medical Director, Trauma Services

N. John Stewart, MD, FACEP
Medical Director, Emergency Medicine

Vince Ford
Vice President, Community Services

The Efficacy Trial of Diaspirin Cross-Linked Hemoglobin(DCLHb) in the Treatment of Severe Traumatic Hemorrhagic Shock

Trauma is the leading cause of death in Americans between the ages of 1 and 44 years and is surpassed only by cancer and artherosclererosis as a cause of death in all age groups. Approximately 60 million injuries occur each year and at least half of these people require medical care; of these 30 million injuries, 3.6 million require hospitalization. Trauma is responsible for 145,000 deaths in the USA each year, frequently from shock that is refractory to resuscitation efforts.

The Trauma Service of Richland Memorial Hospital is excited to be able to inform the medical community about the Service's participation in a multi-centered efficacy study about Diaspirin Cross Linked Hemoglobin (DCLHb). DCLHb is a purified human hemoglobin solution that can be utilized in the treatment of severe traumatic hemorrhagic shock. This solution, unlike traditional blood products, does not require cross-matching and is thus immediately available for infusion in the trauma resuscitation. Blood that has been screened for HIV and Hepatitis viruses is heated and filtered during the pasteurization process to make DCLHb.

DCLHb, in the preliminary studies, has been shown to effectively transport oxygen in vivo as demonstrated by a P50 equal to that of pure human red blood cells. DCLHb has also been shown to optimize vital organ blood flow, prevent tissue hypoxia and lactic acidosis, and ultimately improve survival. DCLHb has also been shown to be effective in small volumes, and thus may improve perfusion in the trauma patient without the untoward effects of large volume crystalloid infusions.

Patients can be enrolled in this efficacy trial if they demonstrate severe shock with signs of hypoperfusion. Patients, such as these, have a projected mortality rate of 40%. The primary purpose of this study will be to determine whether this infusion can reduce 28 day morbidity and mortality following traumatic hemorrhagic shock.

Approximately twenty patients will be enrolled in the study at RMH over a 12 month period, with at least 800 enrolled in 40 centers nationwide. For additional information on this very promising new solution, please contact Dr. Raymond Bynoe, Dr. Richard Bell or Jay Hamm, Trauma Coordinator, at 434-6418.

Trauma Research Study

* Research led by Dr. Raymond Bynoe, Dr. Richard Bell, Stan Fowler of USC and Trauma Services. Expected to begin the end of July or beginning of August.

* RMH is one of 40 sites nationwide.

* Research is using a derivative of human blood products. Will use with patients who have traumatic blood loss and shock. Recipients will have to meet strict criteria. There will be about 1-2 patients per month who will receive the product.

* The product will be given to these patients because they have a high mortality rate, and this product may help them by increasing the body's ability to deliver oxygen to it's cells.

* Secondarily, another benefit may be the possibility that use of the product can extend the community's blood supply.

* We will be informing the community of the study through letters to community leaders and special interest groups and through a press conference either the end of June or beginning of July.

* In other areas, there were a few community concerns about using an "artificial" blood product. This is not an artificial product, it contains human components. Jehovah witnesses can't receive it.

* Another concern to be aware of is the consent process. As in any trauma situation, consent to use the product will be sought from family members, however, the trauma team will use whatever it can to help a person survive. And, that may include use of this product.

* For questions, call Dr. Bynoe's office at 6418.

Questions and Answers
Richland Memorial's Trauma Research Study

Why is this study being performed?

Seriously injured patients frequently arrive at the Trauma Center in shock and suffering from significant blood loss. The purpose of this study is to find out how well the new hemoglobin solution works in treating or preventing the harmful effects of blood loss due to severe injury, including shock, severe illness or death. Approximately 850 patients will take part in this study at 40 hospitals nationwide. Richland Memorial is the first hospital in South Carolina to participate.

What is Diaspirin Cross-Linked Hemoglobin (DCLHb)?

Diaspirin Cross-Linked Hemoglobin is a purified hemoglobin, the part of the blood that carries oxygen. It is made from red blood cells donated by healthy volunteers that have been tested and found negative for the viruses that cause hepatitis and AIDS. In addition, DCLHb solution goes through a specialized filtration and pasteurization process to significantly reduce the risk of hepatitis and AIDS. Because the product can be stored in the Emergency Department, it can be given immediately after a patient's arrival, saving critical moments in stabilizing a trauma patient.

How is the study conducted?

The study is randomized, meaning half the participants will receive the solution and half will receive saline solution. Neither the patient nor the doctor will know which solution the patient will be given. This treatment will be given in addition to standard therapies, not in place of. The trial is authorized by the U.S. Food and Drug Administration (FDA), and will be monitored by an independent data monitoring committee.

Does this replace blood transfusions in the critically injured trauma patient?

No. DCLHb is administered in addition to transfusions that may be needed to treat a patient. Since this product is made from human blood cells, it would not be suitable in treating patients whose religious beliefs forbid blood transfusions. Patients in this study will receive all standard therapies, including blood products, fluids, medications and surgery.

Who will be chosen to participate in this study?

Approximately 20 patients will participate in the study. There is strict medical criteria that the physicians will follow to ensure a patient may participate. Part of the inclusion

criteria includes being 18 years of age or older, evidence of hemorrhage and low blood pressure.

How will a patient know if he or she is receiving the treatment?

Informed consent will be sought from patients if they are conscious and able to make a decision, and/or by family members who will be contacted. Every attempt will be made to obtain consent from the patients, their families or legal representatives before the treatment is given. As with any trauma situation, when a patient is in critical need of immediate attention, the physician will do what is necessary to help the patient survive.

The Food and Drug Administration (FDA), in cooperation with the National Institutes of Health (NIH), issued regulations that allow for certain emergency research to be conducted with an exception from informed consent in rare circumstances when the patient cannot provide consent and the nature of the patient's medical condition requires immediate attention. This study will fit into that criteria. These regulations allow for the advancement of vital emergency research with careful attention to the protection of the rights and welfare of the patients who are enrolled in the study. The FDA and NIH expect that the studies conducted under these rules will allow patients in certain life-threatening situations, who are unable to give informed consent because of their condition, the chance to receive potentially life-saving treatments.

What are the risks and side effects of the treatment?

The product has been extensively studied in randomized trials involving more than 700 patients over a four-year period to evaluate its side effects. Of the approximately 350 patients who have received the treatment, a few temporary side effects were noted, including: temporary and harmless yellowing of the skin, temporary reddening of urine due to the red color of the product, nausea, and back, abdominal and muscle pain.

Who should I contact if I have questions?

If at any time you have questions about the research study, call Dr. Raymond Bynoe, Dr. John Stewart or Jay Hamm of Trauma Services at 434-6418.

Attachment 39

FOR MORE INFORMATION
CONTACT JO HALMES
OR TAMMIE EPPS
PUBLIC RELATIONS, 434-6891

FOR IMMEDIATE RELEASE
June 26, 1997

New, potentially life-saving treatment to be tested at Richland Memorial Hospital

COLUMBIA, S.C. -- Richland Memorial Hospital is one of 40 hospitals nationwide that will begin using a potentially life-saving treatment for patients with severe traumatic injury. The treatment will be available for use beginning in August for patients with severe blood loss secondary to traumatic injuries.

The treatment being researched, Diaspirin Cross-Linked Hemoglobin (DCLHb), is made from human red blood cells.

"We hope the use of this product as a supplement to our life-saving procedures will improve patient outcomes," says Dr. Raymond Bynoe, medical director of Trauma Services and principal investigator of the study. "Despite our best efforts, about 40 percent of trauma patients with extremely low blood pressures, secondary to bleeding problems, die. Large amounts of blood loss can result in lack of oxygen to vital tissues, which can lead to multiple organ failure several days or weeks after the initial trauma.

"DCLHb may increase blood flow and oxygen to vital organs. It also may help us stabilize a patient with severe blood loss."

The DCLHb solution goes through a specialized filtration process to remove hemoglobin, the oxygen-carrying component of the blood. The product is then pasteurized to significantly reduce the risk of viral transmission. Trauma patients must meet strict criteria before being given the new product.

Trauma Services at Richland Memorial treats about 1,500 patients per year. Approximately 20 trauma patients will be eligible to receive the new product in the next 12 months through the study.

"Due to the severity of their injuries, most of these patients will be unable to give informed consent to participate in this valuable project," Bynoe says. "However, every effort will be made to obtain informed consent as soon as possible from either the patient or next of kin. The next of kin or legal guardian may withdraw the patient from the study at any time. This procedure follows the FDA's 'exception from informed consent requirement for emergency research.'"

Bynoe is joined in his research by Dr. N. John Stewart, director of Emergency Services and co-investigator.

"While we are excited about the possibility of this research increasing the survivability of trauma patients, we also are excited about it possibly extending the community's blood supply," Stewart says. "This could help extend our resources nationwide."

If community members are interested in more information about the research project, they may call Trauma Services at 434-6418.

# # #

ERIK CAMPOS/THE STATE

State Treasurer Richard Eckstrom, left, and Comptroller General Earle Morris have apparently ended their 'feud' and cordially joked with other members of the state Budget and Control Board on Tuesday. 'Happy days are here again,' Gov. David Beasley said.

Eckstrom, Morris make peace

"The feud is over; there is no feud. It takes two to feud. And I'm not going to feud. We'll work together. He's a very good man."

STATE TREASURER RICHARD ECKSTROM

By MICHAEL SPONHOUR
Staff Writer

State Treasurer Richard Eckstrom and Comptroller General Earle Morris didn't exactly kiss or hug, but they did call a halt Tuesday to their heated feud.

The rivals shook hands before the opening of the regular meeting of the state Budget and Control Board. They even chatted and shared a laugh.

That's quite a turnaround from last month, when the two men tore each other limb from gut in the media.

"The feud is over; there is no feud," Eckstrom said. "It takes two to feud. And I'm not going to feud. We'll work together. He's a very good man."

The spat has been "media-driven," said Morris, the highest-ranking Democrat in state government.

"Let's end this silliness," he said. "In 45 years, I've gotten along with every elected official in South Carolina. The problem is not me."

In June, Eckstrom called Morris a declining old man gripped by hatred and petty jealousies. Eckstrom said Morris had made an obscenity-laced call to Eckstrom's house late one night after finding out that Eckstrom had removed the comptroller's signature from state checks.

Eckstrom also charged that aides to Morris had spat upon and put chewed gum near his car in the State House garage.

Morris denied those allegations and charged that the first-term Republican was a self-promoter trying to distract attention from a sexual harassment investigation.

Former Eckstrom spokeswoman Leann Register-Johnson has filed a complaint with the Human Affairs Commission charging that she was given poor job evaluations for resisting Eckstrom's attempt to kiss her in January 1996.

Just to make sure peace is maintained, Gov. David Beasley met with the two men privately Tuesday.

"He said to be sweet and kind and to love everybody," said Morris, who still insists that his signature should be on state checks.

Beasley urged the two to give up their ugly feud for the good of the state, said spokesman Gary Karr.

"It's best for both of them to put the past and whatever disputes they have had behind them and to work together whenever they can," Karr said. "These are both good men who have done a lot of good work for South Carolina."

"Let's end t silliness. In years, I've gotten alon with every elected offic in South Carolina."

COMPTROLLER GENE EARLE MORRIS

Richland Memorial to test blood substitute on 20 patients

By LEVONA PAGE
Senior Writer

Over the next year, 20 patients in Richland Memorial Hospital's emergency room will help test a new blood substitute that could eventually relieve worries about tainted transfusions and supply shortages.

The substitute, called Diaspirin Cross-Linked Hemoglobin, will not be used totally instead of normal blood transfusions, but will be used to supplement them.

Patients who will get the blood substitute during the test period are those likely to bleed to death without it, said Dr. Raymond Bynoe, medical director of Trauma Services and principal researcher.

By not having to match blood types or scurry for blood supplies, time can be saved, Bynoe said. "What we are trying to do is help patients who are a high risk for death."

The blood substitute, made by Baxter Healthcare Corp., is a highly filtered and pasteurized hemoglobin, the part of the blood that carries oxygen. The product is made from red blood cells of healthy donors.

A main function of normal blood is to carry oxygen to the vital organs and throughout the body. Because the blood substitute is rich in oxygen, less normal blood would be needed, Bynoe said.

"Instead of using five or six units of blood, we might use two or three," he said. "This will expand our blood supply."

The substitute also could decrease the risk of getting the AIDS virus or hepatitis through blood transfusions because the extra filtering and pasteurization will remove contamination, Bynoe said.

"These additional processes will decrease the risk substantially," he said.

The 20 patients who help test the product might not know in advance that they doing so. When possible, patient or fa consent will be sought, but federal Food Drug Administration rules adopte November allow hospitals to proceed in ous emergencies without consent.

The FDA approval acknowledged that first hour of treatment is crucial in se trauma cases, Bynoe said.

"This is known as the golden hour, we have to be very, very, very aggressiv this time period," he said.

PLEASE SEE **BLOOD** PAGE

BLOOD

FROM PAGE B1

Patients chosen for the test must be at least age 18, have evidence of hemorrhage and low blood pressure, no evidence of pregnancy and no head injury. They will be observed for at least 28 days after the procedure.

Risks are believed to be small, although the FDA has some concerns about the substitute causing hypertension or altered blood flow. Previous trials have produced a few temporary side effects such as yellowing of the skin, reddening of the urine, nausea or pain in the back, abdomen or muscles.

All liability from potential risk is being assumed by Baxter, Bynoe said. Richland is one of 40 hospitals nationwide and the only one in South Carolina participating in the tests, which are to begin in August. Bynoe's partner in the research is Dr. John Stewart, director of Emergency Services at Richland.

About 40 percent of the patients nationwide, or 140,000 to 160,000 people, who enter emergency rooms after severe trauma ultimately die, Bynoe said. If that number can be reduced by 10 percent by using the blood substitute, a significant number of lives will be saved, he said. The search for a substitute for blood goes back to the 17th century, with researchers trying animal blood and wine.

Levona Page can be reached at 771-8512 or by fax at 771-8430.

Attachment 41

000-000201

25

A News Clip From:
Morning News
Florence S.C.
Circ: 33,000
Date of Clip:

JUL - 9 1997

S.C. Press Services Clipping Bureau

New trauma treatment to be tested at Columbia

25

COLUMBIA — Some trauma patients at Richland Memorial Hospital will be getting a new blood product that doctors hope will save lives by providing more of the blood's vital oxygen-carrying component.

The hospital said Tuesday it is one of 40 in the nation testing what is called Diaspirin Cross-Linked Hemoglobin.

Through filtering and pasteurization, the solution concentrates hemoglobin, the blood component that carries oxygen to the body's tissues, while reducing the risk from other blood-borne infections.

Johns Island has

25

A News Clip From:
The Post & Courier
Charleston S.C.
Circ: 110,833
Date of Clip:

JUL - 9 1997

S.C. Press Services Clipping Bureau

Trauma center tries new blood product

25

Associated Press

COLUMBIA — Some trauma patients at Richland Memorial Hospital will be getting a new blood product that doctors hope will save lives by providing more of the blood's vital oxygen-carrying component.

The hospital said Tuesday it is one of 40 in the nation testing what is called Diaspirin Cross-Linked Hemoglobin.

Through filtering and pasteurization, the solution concentrates hemoglobin, the blood component that carries oxygen to the body's tissues, while reducing the risk from other blood-borne infections.

The experimental treatment is designed to increase blood flow and oxygen and stabilize patients who have lost a lot of blood. It will be given in addition to standard treatments, such as transfusions, fluids, medication and surgery.

The hospital said it would do everything possible to get consent from the patient or his or her relatives, but acknowledged that in some cases of extreme injury, that might not be possible before the treatment has to be started.

Richland Memorial's trauma services unit treats about 1,500 patients a year. Hospital officials estimated 20 patients will be eligible for the product during the next 12 months.

Attachment 42

Hospital Liaison Committee *for* Jehovah's Witnesses

Allentown, Pennsylvania

000-000202

SERVING THE LEHIGH VALLEY - NORTHEASTERN PENNSYLVANIA - NORTHWESTERN NEW JERSEY
SHARING RESEARCH ON ALTERNATIVE NON-BLOOD MEDICAL MANAGEMENT

PRESENTATION AG[illegible]

ALLENTOWN, PENNSYLVANIA
HOSPITAL LIAISON COMMITTEE
for
JEHOVAH'S WITNESSES
SERVING THE LEHIGH VALLEY-NORTHEASTERN PENNSYLVANIA
NORTHWESTERN NEW JERSEY

For Emergency and Confidential Use Only

Written Replies to: J. M. Brazil • 3271 Mountain View Dr. • Danielsville, PA 18038-9782

I. Introduction-(2 min)

II. Our Position on Medical Treatment-(3 min)

A. Informed Choice - Not "Right to Die"

III. The Doctor/Patient Relationship-(5 min)

A. Conscience of Doctor/Patient

B. Options for Doctor/Patient

C. Protocol

IV. Acceptable Alternatives to Blood Transfusion (10 min)

A. Nonblood solutions

B. What about blood storage, fractions, serums, autotransfusion?

V. How we Are Set up Internally to Look After Needs of Witnesses

1) Hospital Information Services
2) Hospital Liaison Committee
3) Visitation groups
4) Ongoing education

VI. A Sensitive Matter: Treatment of Children-(7 min)

A. Parental responsibility

B. Legal issues

C. Doctor's options

VII. Conclusion-(1 min)

VIII. Questions and Answer Session-(15 min)

ALLENTOWN, PENNSYLVANIA HOSPITAL LIAISON COMMITTEE *for* JEHOVAH'S WITNESSES

SERVING THE LEHIGH VALLEY-NORTHEASTERN PENNSYLVANIA
NORTHWESTERN NEW JERSEY

For Emergency and Confidential Use Only

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